Osteoporosis Prevention in Premenopausal Women and Children

By

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Submitted in fulfillment of the requirements for the Degree of

Doctor of Philosophy

University of Tasmania (March, 2006)

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Abstract

Osteoporosis Prevention in Premenopausal Women and Children

Maximising peak bone mass, and reducing premenopausal bone loss are both potential approaches for the long-term prevention of osteoporosis and fracture. However, little is known about how to improve osteoporosis preventive behaviours in either premenopausal women or children.

We performed a randomised controlled trial of individualised bone density feedback combined with either a leaflet or group education (the Osteoporosis Prevention and Self-management Course ((OPSMC)) in 467 healthy premenopausal women. Outcomes measured included changes in calcium intake; physical activity and fitness; BMD at the femoral neck and lumbar spine; osteoporosis knowledge and self-efficacy; and, maternal report of changing children's calcium intake and physical activity.

Key findings were:

- Feedback of low BMD resulted in a greater increase in femoral neck (but not lumbar spine) BMD compared to feedback of normal BMD (1.6% p.a. vs. 0.7% p.a., p=0.0001).
- Participation in the OPSMC had no greater effect on BMD than receiving a simple leaflet.
- Femoral neck BMD change was associated with starting calcium supplements (1.3 % p.a, 95%CI +0.49, +2.17) and self-reported change in physical activity levels (0.7% p.a., 95%CI +0.22, +1.22).

- Both the OPSMC and feedback of low T-score were associated with long-term improvements in osteoporosis knowledge, but not self-efficacy.
- Mother's report of increasing their children's calcium intake was associated with receiving the OPSMC (OR 2.3, 95%CI 1.4,3.8) and feedback of a low T-score (OR 2.0, 95%CI 1.2,3.3).

We also performed a systematic review of the effects of calcium supplementation in children, which found that supplementation had effects only on total body bone mineral content (standardised mean difference (SMD) +0.14, 95% CI+0.01, +0.27) and upper limb BMD (SMD +0.14, 95%CI +0.04, +0.24). This small treatment effect, if applied to the peak incidence of childhood fractures, would result in a decrease in absolute risk of at most 0.2% p.a. in boys and 0.1% p.a. in girls.

In conclusion, individualised BMD feedback combined with a minimal educational intervention is effective at increasing hip but not spine bone density in premenopausal women. The changes in behaviour through which this was mediated are potentially important in the prevention of other diseases, thus measuring BMD at a young age may have substantial public health benefits, particularly if these changes are sustained. The apparent effect of bone density feedback and the OPSMC delivered to mothers on osteoporosis preventive behaviours in their children could add to the public health benefits of such interventions. However, further research using objective measures of children's behaviour change is needed to confirm this finding. While it is possible that the small increase in BMD from calcium supplementation seen in the systematic review could reduce fracture risk in childhood, the public health impact of this appears small. Alternative methods of achieving osteoporosis preventive behaviours in children need further exploration.

Acknowledgements

The study into bone density feedback in premenopausal women was funded through an National Health and Medical Research Council project grant.

I am very grateful to the Department of Health and Human Services, Government of Tasmania for their support through the Dick Buttfield Memorial Fellowship, which enabled me to pursue my PhD full-time. I hope that through the research presented in this thesis I can demonstrate the value of their support and I sincerely hope that I can continue to do so through developing an ongoing research career to benefit the Tasmanian community.

Thank you to Osteoporosis Australia for the use of the Osteoporosis Prevention and Self-management Course in our study.

I am also extremely grateful to my supervisor, Professor Graeme Jones for giving me such an enjoyable and valuable learning experience throughout my PhD. I am sure he is aware of the critical intellectual input he has had into this thesis, but I would also like to acknowledge some other key attributes which he has shown which have added to the value of my PhD training. These include: strategic thinking re research directions and publication; encouragement of independent projects and of forming collaborations outside the Menzies Research Institute; and recognising the importance of balancing a commitment and passion for research with other important parts of life.

Research is a team activity and I thank the entire team at the Menzies Research Institute for support, advice and assistance throughout my time here. In particular to Tim Albion and the IT team for rapid assistance whenever it has been required, to Leigh Blizzard and the statistical team for being so approachable and helpful, Kathy Thomson who has always advised me well regarding the practical logistics of performing research and Laura De Wit, whose terrific rapport with the study participants is apparent in their ongoing readiness to support our work. The study participants themselves deserve thanks for being so generous of their time to support our work. I would also like to thank our collaborators on the project, Prof Brian Oldenburg and Dr Malcolm Riley, for their contributions to this study.

I acknowledge the support of the Cochrane Musculoskeletal group throughout the process of the systematic review component of this thesis, especially Lara Maxwell for her prompt answers to my many calls for help and to Louise Falzon for performing the literature search on my behalf.

And lastly, but very importantly, thank you to my partner Lise, and my four-legged family, none of whom turned a hair when I changed career and income level to pursue my long-term goal of a research career.

List of Publications

Publications arising from the thesis:

Chapter 4:

Winzenberg T, Oldenburg B, Frendin S, Jones G. The design of a valid and reliable questionnaire to measure osteoporosis knowledge in women: the Osteoporosis Knowledge Assessment Tool (OKAT). BMC Musculoskeletal 2003;4(1):17.

Chapter 5:

Winzenberg TM, Riley M, Frendin S, Oldenburg B, Jones G. Sociodemographic factors associated with calcium intake in premenopausal women: a cross-sectional study. Eur J Clin Nutr 2005;59(3):463-66.

Chapter 6:

Winzenberg TM, Oldenburg B, Frendin S, De Wit L, Jones G. Effects of bone density feedback and group education on osteoporosis knowledge and osteoporosis self-efficacy in premenopausal women: a randomized controlled trial. J Clin Densitom 2005;8(1):95-103.

Chapter 7:

Winzenberg T, Oldenburg B, Frendin S, De Wit L, Riley M, Jones G. The effect on behavior and bone mineral density of individualized bone mineral density feedback and educational interventions in premenopausal women: a randomized controlled trial [NCT00273260]. BMC Public Health 2006;6(1):12.

Chapter 8:

Winzenberg TM, Oldenburg B, Frendin S, De Wit L, Jones G. A mother-based intervention trial for osteoporosis prevention in children. Prev Med 2006;42(1):21-6.

Chapter 9:

How do women change osteoporosis preventive behaviours in their children?

Winzenberg T, Hansen E, Jones G. Submitted European Journal of Clinical Nutrition.

Chapter 10:

Winzenberg TM, Jones G, Shaw K. Calcium supplementation for improving bone mineral density in children. (Protocol). The Cochrane Database of Systematic Reviews 2005;2005(1):Art. No.: CD005119. DOI: 10.1002/14651858.CD005119.

Winzenberg TM, Jones G, Shaw K. Calcium supplementation for improving bone mineral density in children. (Review). Accepted Cochrane Database of Systematic Reviews.

Scientific presentations arising from the thesis:

1. Winzenberg,T, Hansen, E, Jones,G. How do women change osteoporosis preventive behaviours in their children? Poster: Nutrition Society of Australia ASM, 2005.
2. Winzenberg,T, Shaw,K, Fryer,J, Jones, G. Calcium supplementation for improving bone mineral density in children: a systematic review. Oral: Nutrition Society of Australia ASM, 2005
3. Winzenberg,T, Shaw,K, Fryer,J, Jones, G. Calcium supplementation for improving bone mineral density in children: a systematic review. Plenary Oral: Australian New Zealand Bone Mineral Research Society Annual Scientific Meeting (ASM) 2005
4. Winzenberg,TM, Frendin, S, Oldenburg, BO, Jones, G. The Effect of Bone Mineral Density Feedback and Group Education on Osteoporosis Preventive Behaviour and Bone Mineral Density in Premenopausal Women: A Randomised Controlled Trial. Oral: Australian New Zealand Bone Mineral Research Society ASM 2004.
5. Winzenberg,TM, Oldenburg, BO, Frendin, S, De Wit, L , Jones, G. Educating mothers can alter children's osteoporosis preventive behaviours. Poster: Australian New Zealand Bone Mineral Research Society ASM 2004.
6. Winzenberg,TM, Frendin, S, Oldenburg, BO, Jones, G. The Effect of Bone Mineral Density Feedback and Group Education on Osteoporosis Preventive Behaviour and Bone Mineral Density in Premenopausal Women: A Randomised Controlled Trial. Poster: American Society for Bone Mineral Research 25th Annual Meeting, 2003.
7. Winzenberg,TM, Frendin, S, Oldenburg, BO, Jones, G. Bone mineral density feedback combined with a simple education intervention causes an increase in bone mineral density in premenopausal women. Oral: RACGP 46th National Convention and AGM, 2003.

8. Winzenberg TM, Riley M, Frendin S, Oldenburg B, Jones G. Sociodemographic factors associated with calcium intake in premenopausal women: a cross-sectional study. Oral: Nutrition Society of Australia ASM, 2003.
9. Winzenberg, TM, Oldenburg, B, Frendin, S, Jones, G. Effects of bone density feedback and small group education on osteoporosis knowledge and self-efficacy in pre-menopausal women. Poster: Australian New Zealand Bone Mineral Research Society ASM 2003.
10. Winzenberg, TM, Riley M, Frendin S, Oldenburg B, Jones G. Factors associated with total calcium intake in premenopausal women: a cross-sectional study. Poster: Australian New Zealand Bone Mineral Research Society ASM 2002.

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List of Abbreviations

BMC	Bone mineral content
BMD	Bone mineral density
CI	Confidence interval
DALY	Disability adjusted life years
DPA	Dual photon absorptiometry
DXA	Dual energy x-ray absorptiometry
IU	International units
OKAT	Osteoporosis knowledge assessment tool
OPSMC	Osteoporosis prevention and self-management course
OR	Odds ratio
p.a.	Per annum
RDI	Recommended dietary intake
SD	Standard deviation
SMD	Standardised mean difference
SPA	Single photon absorptiometry
UK	United Kingdom
US	United States

Synopsis

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. It is a major and growing public health problem, particularly in women and is a significant problem both in Australia and internationally. Maximising peak bone mass, and reducing premenopausal bone loss are both potential approaches for the long-term prevention of osteoporosis and fracture. However, little is known about how to improve osteoporosis preventive behaviours in either premenopausal women or children. This thesis explores approaches to changing osteoporosis preventive behaviours in premenopausal women to reduce premenopausal bone loss, and approaches to improving peak bone mass in children through lifestyle interventions and direct intervention through calcium supplementation.

Chapter 1 is a review of the literature relating to osteoporosis to provide appropriate background for the studies in the thesis. It discusses the public health importance of osteoporosis; bone acquisition and changes in bone mineral density over different life stages and its implications for osteoporosis prevention; and, the health impacts on bone and on prevention of chronic diseases of modifiable lifestyle factors affecting osteoporosis. It also reviews the literature pertaining to changing osteoporosis preventive behaviours in premenopausal women and children, including two key concepts from the health promotion literature in this area namely, osteoporosis knowledge and osteoporosis self-efficacy.

Chapter 2 describes the research questions.

Chapter 3 describes the research methodology for the clinical trial which forms the main component of this thesis. The results of the study are described in subsequent chapters.

Chapter 4 describes the development of and psychometric properties of a survey instrument specifically developed to measure osteoporosis knowledge in this study, the Osteoporosis Knowledge Assessment Tool (OKAT). This 20-item instrument with true, false and don't know responses was drafted based on Osteoporosis Australia's Osteoporosis Prevention and Self-management Course (OPSMC) and the information leaflet "Understanding Osteoporosis". The scoring range was 1 to 20. It was administered to the entire study sample of 467 randomly-selected, healthy women aged 25-44 years. Questionnaire performance was assessed by Flesch reading ease, index of difficulty, Ferguson's sigma, inter-item and item-total correlations, Cronbach's alpha and principal component factor analysis. The Flesch reading ease was higher than desirable at 45, but this was due to the use of the word osteoporosis in many items. Of the individual items 17 had an index of difficulty less than 0.75. The questionnaire had a Ferguson's sigma of 0.96, a Cronbach's alpha of 0.70 and factor analysis consistent with only one factor (osteoporosis knowledge) being measured. Levels of osteoporosis knowledge were low with a mean score of 8.8 out of 20 which suggests the OKAT may be sensitive to change. The OKAT has good psychometric properties for measuring osteoporosis knowledge in Australian 25-44 year old females. While it should be applicable to other Caucasian populations, this will require confirmation by further research.

Chapter 5 reports the results of a cross-sectional analysis performed on the study cohort aiming to describe the associations between sociodemographic factors and calcium intake in pre-menopausal women and to determine the effect of having low milk intake on meeting the recommended dietary intake (RDI) for calcium. This found that daily total calcium intake was 789 mg (IQR 511 to 983). Education level, calcium-specific osteoporosis knowledge and self-efficacy were all independently associated with calcium intake ($p<0.05$). There were no associations between calcium intake and hours of employment, smoking history, marital status, age, family or personal history of fracture, number of children or having ever breastfed. The odds of achieving the RDI for calcium increased with higher levels of calcium-specific self-efficacy and knowledge, and decreased in current smokers or if the main financial provider in the household was unemployed ($p<0.05$). Women drinking more than 300 ml of milk per day were more likely to meet the RDI for calcium (OR 11.1,95%CI 6.6-18.7). In conclusion, women who have lower levels of education, who are in households where the main financial provider is unemployed, who are smokers, and those with low levels of calcium-specific self-efficacy and knowledge, are at risk of not achieving adequate calcium intake. This information will inform public health strategies aimed at improving the calcium intake of women in this age group.

In **Chapter 6**, the impact of a randomised controlled trial of individualised bone density feedback and two different educational interventions (an osteoporosis information leaflet and group-based behavioural education (the OPSMC)) on osteoporosis knowledge and self-efficacy in 470 women aged 25-44 years are examined. Osteoporosis knowledge increased across all intervention groups. Women receiving the OPSMC had a greater increase in both short ($\beta = +1.33$, 95% CI +0.72, +1.94) and

long-term (β = +0.64, 95%CI +0.0034, +1.25) osteoporosis knowledge, compared to those receiving the leaflet. In contrast, a low T-score was associated with a significant increase in long-term (β = +0.66, 95%CI +0.0034, +1.25) but not short-term (β = +0.57, 95%CI -0.036, +1.17) osteoporosis knowledge, compared to a normal T-score. Changes in osteoporosis self-efficacy were not associated with either low BMD or receiving the OPSMC but were negatively associated with number of children (β = -0.9, 95%CI –1.4, -0.3) and working more than 20 hours per week (β = -2.7, 95%CI –4.6, -0.8). In conclusion, both the OPSMC and bone density feedback increased osteoporosis knowledge but not self-efficacy over two years. Women with children or who worked full-time have decreased osteoporosis self-efficacy, suggesting that this group should be a specific target for future interventional strategies.

Chapter 7 describes the effects of individualised bone density feedback and the two different educational interventions described above on osteoporosis preventive behaviour and bone mineral density (BMD) in pre-menopausal women over a 2-year period. Main outcome measures were dietary calcium intake, calcium supplement use, smoking behaviour, physical activity, endurance fitness, lower limb strength and BMD. Women who had feedback of low BMD had a greater increase in femoral neck BMD than those with normal BMD (1.6% p.a. vs. 0.7% p.a., p=0.0001), but there was no difference in lumbar spine BMD change between these groups (0.1% p.a. vs. 0.08% p.a., p=0.9). Both educational interventions had similar increases in femoral neck BMD (Leaflet = +1.0% p.a., Osteoporosis self-management course = + 1.3% p.a., p=0.4). Femoral neck BMD change was only significantly associated with starting calcium supplements (1.3 % p.a, 95%CI +0.49, +2.17) and persistent self-reported change in physical activity levels (0.7% p.a., 95%CI +0.22, +1.22). These results demonstrate

that individualised BMD feedback combined with a minimal educational intervention is effective at increasing hip but not spine bone density in premenopausal women. The changes in behaviour through which this was mediated are potentially important in the prevention of other diseases, thus measuring BMD at a young age may have substantial public health benefits, particularly if these changes are sustained.

Chapter 8 gives the results of an additional analysis designed to explore whether a lifestyle intervention delivered to mothers might impact on osteoporosis preventive behaviours in their children. As part of the same randomised controlled trial described above, we assessed maternal report of children's calcium intake and physical activity change in the 354 mothers in the study sample. Receiving small group education was associated with mothers' report of increasing children's calcium intake (odds ratio 2.3, 95% confidence interval 1.4, 3.8), as was low T-score feedback (odds ratio 2.0, 95% confidence interval 1.2, 3.3). Mothers who increased their own physical activity were more often reported increasing both physical activity (odds ratio 2.7, 95% confidence interval 1.5, 5.0) and calcium intake in their children (odds ratio 2.2, 95% confidence interval 1.3, 3.7). Mothers who commenced calcium supplements more often reported increasing children's calcium intake (odds ratio 2.6, 95% confidence interval 1.0, 6.7) but not physical activity. Both bone mineral density feedback and small group education delivered to mothers are effective at inducing maternally-reported osteoporosis preventive behaviour change in their children. These results require confirmation by studies with objective outcome measures.

Chapter 9 describes a qualitative study performed to explore the approaches taken to changing these behaviours in their children were unknown. We aimed to describe the

strategies and approaches used, in order to inform the development of practical and efficacious health promotion strategies in children. Semi-structured interviews were performed in a purposively selected sub-sample of 39 mothers taken from the original random population-based sample of 354 mothers described in chapter 8. These mothers described a variety of specific dietary changes they made to increase their children's calcium intake. They also described general approaches to improving both calcium intake and physical activity such as: raising awareness of the importance of calcium; ensuring calcium-rich foods were accessible; assessing their children's likes and dislikes and working within these; role modeling; information provision; taking a balanced approach to attempting behaviour change; and encouraging activities that they could do with their children. Mothers described the general importance of a having a balanced diet and lifestyle, rather than specifically for osteoporosis. These results demonstrate that even without specific guidance, mothers are adept at identifying barriers to change and developing strategies to apply to changing lifestyle behaviours in their children. The results also provide information which could be incorporated into future interventions for lifestyle change in children and provide further support for considering parent-focused approaches to this problem.

Chapter 10, describes a systematic review of calcium supplementation for improving bone density in children. The review aims were:

- To determine the effectiveness of calcium supplementation for improving BMD in children; and
- To determine if any effect varies by sex, pubertal stage, ethnicity or level of physical activity, and if any effect persists after supplementation is ceased.

We performed a comprehensive and systematic search of the literature using multiple databases and hand-searching to identify potential studies. Studies included were randomised controlled trials of calcium supplementation (including by food sources) compared with placebo, with a treatment period of at least 3 months in children without co-existent medical conditions affecting bone metabolism. Bone outcomes had to be measured after at least 6 months of follow-up. The 19 trials included involved 2859 participants. There was no effect of calcium supplementation on femoral neck or lumbar spine BMD. There was a small effect on total body BMC (SMD +0.14, 95% CI+0.01, +0.27) and upper limb BMD (SMD +0.14, 95%CI +0.04, +0.24). Only the effect in the upper limb persisted after supplementation ceased (SMD+0.14, 95%CI+0.01, +0.28). This effect is approximately equivalent to a 1.8% greater increase in supplemented groups. There was no effect modification by baseline calcium intake, sex, ethnicity, physical activity or pubertal stage. We concluded that while there is a small effect of calcium supplementation in the upper limb, the increase in BMD which results is unlikely to result in a clinically significant decrease in fracture risk. The results do not support the use of calcium supplementation in healthy children as a public health intervention. These results cannot be extrapolated to children with medical conditions affecting bone metabolism.

Chapter 11 summarises the findings of the thesis and suggests directions for future research.

Chapter 1: Literature Review

1.1 Osteoporosis and its public health importance

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and micro-architectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture [1]. It is a major and growing public health problem, particularly in women [2, 3] and is a significant public health problem both in Australia and internationally. This is because it is both a common disease, and a disease with significant associated morbidity, mortality and economic costs mainly as a consequence of the occurrence of fragility fractures.

Approximately 1.9 million people in Australia were affected by osteoporosis in 2001 [4] of whom about one quarter are male. The prevalence is likely to increase over time as the population ages, to an estimated 3 million people by 2021 [4]. Osteoporotic fractures in Australia are common. Estimated residual lifetime risk estimates in Australian populations have varied in different cohorts but have been uniformly high. In the Dubbo Osteoporosis Epidemiology study estimates were 29% for men and 56% for women aged over 60 [3]; in the Tasmanian Older Adult Cohort estimates were 27% for men and 44% for women aged over 50 [2]; and in the Geelong Osteoporosis study it was estimated that lifetime risk of fracture for women aged over 50 years was 42% [5]. In terms of morbidity and mortality, the years of healthy life lost in Australia due to osteoporosis in 2001 were estimated as over 25,000 disability adjusted life years (DALYs), of which over a half were lost due to premature death [4]. The predicted annual direct treatment costs in Australia in 1992 for atraumatic fractures occurring in subjects older than 60 years was estimated as $A779 million or approximately $A44 million per million of population per annum. The majority of direct costs (95%) were

incurred by hospitalized patients and related to hospital and rehabilitation costs [6]. In 2001, these direct financial costs were estimated to be $A1.9 billion and indirect costs to be about $A5.57 billion [4].

These significant impacts are also found internationally. In a study aimed at quantifying the global burden of hip fracture, Johnell and Kanis estimated that in 1990 there were 1.31 million new hip fractures and the prevalence of hip fractures with a disability was 4.48 million. There were 740, 000 deaths estimated to be associated with hip fracture and 1.75 million DALYs lost [7]. This represents 0.1% of the global burden of disease and 1.4% of the burden from the established market economies (including North America, Japan, Australasia and Western Europe). The impact of vertebral fractures has been studied less [8]. However, it is clear that vertebral fracture adds significantly to the burden of osteoporosis. For example, the number of prevalent vertebral fractures in the European Community is expected to rise from 23.7 million in 2000 to 37.3 million by 2050 and the total cost of vertebral fractures in the European Union was estimated as 377 million Euros in 2001 [9].

Osteoporosis prevention has been widely recognized as a public health priority. In Australia, the high prevalence and costs of osteoporosis have led to 2001-2010 being labeled the Bone and Joint Decade and musculoskeletal disorders being recognised as a national health priority with osteoporosis being one of the 3 musculoskeletal conditions included in the Arthritis and Musculoskeletal Conditions National Action Plan. Other examples of similar recognition include Europe's Osteoporosis in the European Community Action Plan [10] and the United States' declaration of 2002-2011 as the Decade of the Bone and Joint.

1.2 Bone acquisition and changes in bone mineral density over life stages

1.2.1 Childhood and adolescence

The full-grown fetus at term contains about 21 g (range 13-31 g) of calcium [11]. Based on a cross-sectional study of infants aged 1 to 391 days, whole body BMC increases by 389% and total body BMD increases by 157% during infancy [12]. While bone mass increases occur throughout childhood, puberty is a key stage for bone mass acquisition with skeletal mass approximately doubling between the onset of puberty and young adulthood [13]. At least 90% of peak bone mass is obtained by age 18 years [14]. The pattern in bone growth in boys differs from that in girls in two ways [15]. Puberty is of later onset in boys (age 14 years compared to 12 years) resulting in a longer period of prepubertal growth. The pubertal growth spurt in boys is also longer, lasting 4 years compared to 3 in girls. This results in boys having a greater peak bone mass. Peak bone mineral content velocity occurs approximately 6-7 months later than peak height velocity [14, 16]. The time peak bone mass is reached has been estimated to be as early as 16-18 years at the lumbar spine and femoral neck or mid-shaft femur, and as late as age 35 at the radius, skull and whole body [17].

1.2.2 Premenopausal Bone loss

Longitudinal studies examining the natural history of BMD loss in Caucasian populations have been consistent with there being onset of bone loss in the pre-menopausal period [18-23]. The time at which this loss begins after attainment of peak

bone mass is not clear. Slemenda reported bone loss from the hip at a rate of 0.3% per year in 96 premenopausal women (defined as age 30-45 with follicular stimulating hormone < 15 mIU and with regular menstrual cycles) but no bone loss from the lumbar spine in this group of women [19]. Riggs reported lumbar spine bone loss of 1.27% p.a. in premenopausal women taken from a cohort of 20 to 88 year old women. A larger study (n=614) in 24 to 44 year old women reported annual loss of BMD at the femoral neck BMD of about 0.3 % of baseline BMD p.a., and bone loss potentially beginning as early as age 24 [21]. In the same study, the onset of lumbar spine bone loss was estimated at 38-39 years, with the maximum annual loss being 0.5% p.a. Other estimates of premenopausal lumbar spine BMD loss have been 0.79% p.a.[22] and 0.82% p.a. [23].

In the single longitudinal study that did not demonstrate statistically significant lumbar spine bone loss in the premenopausal period [24] (mean age 45.7 years, SD 0.4 years), lumbar spine loss over a 12 month period of observation was –0.2 % (95% CI –0.9, +0.4) in women with regular menses. While this was not statistically significant, the subgroup of premenopausal women was small (n=36) and the point estimate consistent with other positive studies, so that this may be an effect of lack of study power rather than the absence of real premenopausal lumbar spine bone loss.

1.2.3 Effect of Menopause and Age-related Bone Loss

Evidence from cross-sectional studies indicates that bone loss occurs exponentially after menopause [25, 26]. For total bone calcium, 12 % is lost in the 25 years after menopause and up to 50% of this loss occurs in the first ten years post-menopause [26]. At the femoral neck, 11% of BMD was lost by 5 years, 16% by 10 years and 20% by 20 years

post-menopause. Recker et al [27] performed a longitudinal study of bone loss in women aged older than 46 years. In this study, a sigmoid pattern of bone loss across menopause was described, beginning 2-3 years prior to last menses and ending 3-4 years after the last menses. Total oestrogen-deprivation bone losses over this period were estimated as 10.5, 7.73 and 5.3 % for the spine, total body bone mineral and femoral neck respectively.

A 4- year study in peri- and post-menopausal women who at follow-up were on average 13.6 years since menopause, demonstrated an annual change in lumbar spine bone mass in women not on hormone replacement therapy of -0.39% ($P < 0.02$) and an annual change at the femoral neck of -0.51% ($P < 0.01$) [28]. The femoral neck finding but not the lumbar spine is similar to that of Recker et al [27] who found that after completion of the menopausal drop, bone losses were linear, with a loss of 0% p.a. at the lumbar spine, -0.6% p.a. for the total body and –0.45% p.a. for the femoral neck, which were described as age-related bone losses. The authors suggested that extrapolating this data out to age 75 years would indicate a loss of 22% for the total body and 19% at the femoral neck. However, the rates of bone loss in the 8th and 9th decade may be higher than reported in this study. In a longitudinal study of 5689 women over age 65 at baseline [29], the rate of decline in total hip BMD steadily increased from 2.5 mg/cm^2/year (95% confidence interval 2.0 to 2.9) in women 67-69 years old to 10.4 mg/cm^2/year in those aged 85 or older (95% confidence interval 8.4 to 12.4). The rate of bone loss also increased with aging at all sub- regions of the hip and at the calcaneus.

1.2.4 Implications for the Timing of Osteoporosis Prevention

BMD in later life is a function of peak bone mass and the rate of subsequent bone loss [30, 31]. This has implications for decisions about when to attempt interventions to prevent osteoporosis and resultant osteoporotic fractures. One approach is to take the point of view that osteoporosis is a disease with its origins in childhood [32], and therefore efforts should be made to determine how to maximise peak bone mass. This has been supported by modeling which indicates that a 10% increase in peak bone mass is predicted to delay the onset of osteoporosis by 13 years [33]. Another approach is to concentrate on prevention of bone loss at menopause and in old age. However, it is estimated that over their lifespan women lose approximately 42% of their spinal and 58% of their femoral bone mass [34] and as described above, although bone mineral density is lost most rapidly post-menopausally, a substantial amount of this bone loss occurs pre-menopause. Furthermore, premenopausal bone mass contributes to fracture risk in later life [31]. If premenopausal bone loss can be reduced, or potentially reversed, then this has important implications for the long-term prevention of osteoporosis and fracture. A decrease of only 10% in non-menopausal bone loss is predicted to delay the onset of osteoporosis by approximately 2 years [33]. The remainder of this thesis concentrates on issues related to osteoporosis prevention in premenopausal women and children.

1.3 Health Impacts of Modifiable Lifestyle Factors Affecting Osteoporosis

1.3.1 Risk factors for osteoporosis in women.

Risk factors for osteoporosis in women [11] are given in Table 1. In addition to these risk factors, vitamin D levels [35] and levels of physical activity [36] are also implicated in bone health. Of these risk factors, key, modifiable lifestyle factors for the prevention of osteoporosis include calcium intake and physical inactivity in adults and children, and cigarette smoking [37] in adults.

Table 1: Risk factors for osteoporosis and fracture in women

Age
Genetic
White or Asian ethnicity
Family history of osteoporosis
Small body size/weight
Hormonal
Late menarche (> 15 years)
Prolonged amenorrhoea
Premature or surgical menopause
Lifestyle/nutrition
Inadequate calcium intake
Smoking
Alcoholism
Illnesses/Diseases
Eating disorders
Hyperthyroidism
Hyperparathyroidism
Glucorticoid excess
Malabsorption eg coeliac disease
Liver disease
Rheumatoid arthritis
Depression
Medications
Anticonvulsants
Glucorticoids
Heparin
Chemotherapeutic agents
Warfarin

1.3.2 Effects on bone of calcium intake and physical activity in childhood

Low bone mineral density (BMD) is a major risk factor for osteoporotic fracture [38, 39]. As described above, BMD in later life is a function of peak bone mass and the rate of subsequent bone loss [30]. Maximizing peak bone mass is one potential way to reduce the impact of age-related bone loss [40](in press). Influences on peak bone mass include genetic factors [41], nutrition (especially calcium intake [42]) and physical activity [42-44]. Therefore, one potential effect of improving osteoporosis preventive behaviours in childhood, particularly calcium intake and physical activity levels, is to improve peak bone mass. In addition, there is evidence that low BMD in childhood is itself a risk factor for fractures occurring in childhood [45-47], suggesting that optimising age-appropriate bone mass may also have a more immediate preventive effect on fracture rates in children.

There is evidence that dietary and physical activity behaviours may track from childhood to adulthood [48-50]. Therefore, changing osteoporosis preventive behaviours in childhood may have an ongoing positive effect on these behaviours in adult life, with potential to prevent or reduce age-related bone loss and subsequently fracture, as discussed below.

1.3.3 Effects on bone of smoking, calcium intake and physical activity behaviours in premenopausal women

As discussed above, smoking, calcium intake and physical activity behaviours have been implicated in bone health in adult life.

Smoking has been implicated in both low BMD and increased fracture rates in post-menopausal women [37], but the impact of smoking in younger women is less clear. A meta-analysis of cross-sectional studies suggested that smoking had no effect on BMD in pre-menopausal women. However, this meta-analysis did not report on the presence or absence of heterogeneity in results, nor on the possibility of effect modification by other factors. Results from individual cross-sectional studies are inconsistent with some [51-57] reporting a negative association of smoking with BMD and others [58-60] not. It has been suggested that the inconsistency may be due to effect modification by other factors [61] and in fact effect modification by BMI, breastfeeding and sports participation [61] and by fat mass [62] has been reported. One longitudinal study which included premenopausal women [63] reported the presence of a negative effect of smoking in the premenopausal women, another did not [64]. Therefore, while the evidence is less than for older women, it is sufficient to suggest that smoking may have a negative impact effect on BMD even in premenopausal women, even if only in certain subgroups, such as women with low BMI.

Evidence relating to the effects of improving calcium intake and physical activity in premenopausal women is clearer. The treatment effect in premenopausal women reported from a meta-analysis of randomised controlled trials of calcium supplementation was 1.1% p.a. at all bone sites except the ulna. In cross-sectional studies, the correlation between calcium intake and bone mass was also significant (0.12, 95%CI 0.09, 0.16) [65]. A meta-analysis of exercise interventions in premenopausal women reported a treatment effect of 0.9 % p.a. at both the femoral neck and lumbar spine [66]. The studies included in this meta-analysis used interventions

including both high-impact and resistance exercise. Similar effect sizes have been reported in other later trials of high-impact exercise in premenopausal women [67, 68]. However, a small meta-analysis of individual patient data (n= 143 patients) of resistance exercise did not show any statistically significant effect of lumbar spine of femoral neck BMD change [69], indicating that the type of physical activity may be a consideration for osteoporosis prevention. Numerous cross-sectional studies have also reported a positive association with physical activity and bone density measures [70-79].

1.3.4 Impact of calcium intake, physical activity and smoking on other chronic diseases.

Low calcium intake and low levels of physical activity have been implicated in the causation of a large number of chronic illnesses in both childhood and adulthood and the impact of smoking on health in adults is well-known.

1.3.4.1 Effects of calcium intake and physical activity on childhood health

Besides potential benefits for bone health, there are other possible more immediate beneficial effects of adequate calcium intake and physical activity levels in childhood. Calcium intake and dairy product consumption measured longitudinally have been shown to be inversely related to percent body fat in children [80, 81] and reduced physical activity energy expenditure may also play a role in weight gain in children over time [82]. Conversely, exercise interventions have been shown to reduce percent body fat, fat-free mass, body mass and BMI [83], particularly low-intensity, long-duration exercise; aerobic

exercise combined with high repetition resistance training and exercise program combined with a behavioural-modification component. Given that childhood overweight and obesity is estimated to be present in over 20% of Australian children [82] and 29% of Tasmania children [84], and that this figure is increasing [82], changing behaviours that influence development of these conditions is of great public health importance. Other beneficial effects in childhood from increased childhood physical activity may include improved blood pressure, and social-psychological benefits such as reduced symptoms of depression, stress and anxiety and positive effects on self-concept [85]. There is also evidence that physical activity may be inversely associated with i.e. protective against, cigarette smoking, alcohol use and use of illegal drugs [85].

1.3.4.2 Effects of calcium intake, physical activity and smoking on adult health

Importantly, a diet containing adequate calcium and maintaining adequate levels of physical activity also have benefits for chronic diseases in adulthood. There are potentially beneficial roles for calcium intake in diseases including, hypertension [86], obesity [87-89], colon cancer [90-92], ovarian cancer [93], hypercholesterolaemia [94, 95], breast cancer [96], pre-eclampsia [97] and premenstrual syndrome [98, 99]. Similarly, physical activity reduces all cause mortality and has beneficial effects for diseases such as cardiovascular disease, hypertension, non-insulin-dependent diabetes mellitus and obesity, relieves symptoms of depression and anxiety and improves mood, and may be beneficial for breast cancer prevention [100] and for prevention of pre-eclampsia [101] and colon cancer [100, 102]. The health effects of smoking are well-documented and wide-ranging [103] and include cancers (bladder, cervical, oesophageal, kidney, laryngeal, lung, oral,

pancreatic, stomach cancers and leukaemia), cardiovascular disease, respiratory diseases, reproductive effects (SIDS, reduced fertility, low birth weight and pregnancy complications) and cataracts.

1.3.5 Calcium intake and physical activity in children

Recommendations for calcium intake [104] and proposed recommendations for physical activity [85] in children in Australia are described in Tables 2 and 3. Despite the increasing evidence for both short and long term benefits of adequate calcium intake and physical activity in children, the prevalence of low levels of calcium intake and low levels of physical activity remains high, the latter particularly in older children. In Australia, 25-50% of boys depending on age group fail to meet the recommended dietary intake (RDI) for calcium, and at least 50% of girls at any age fail to meet the RDI, with this rising to 75% for girls aged 12-15 [105]. A recent physical activity survey in Melbourne children [106] demonstrated that the average time spent in moderate to vigorous physical activity per day was 4.1- 4.5 hours at age 5-6 years but this declined to 2-2.4 hours per day by age 10-12 years. Children aged 5-6 and 10-12 years spent a mean of approximately 5.8 hours and 6.7 hours respectively in sedentary activities daily. Tasmanian children aged 9-16 spend an average of 2-3 hours daily on television, computer and video viewing alone [84]. There is therefore scope for substantial improvement in both calcium intake and physical activity behaviours in Australian children.

Table 2: Australian Recommended Daily Intakes for Calcium intake in Children

Age	Calcium intake mg/day
Infants (0-6 months)	
Breastfed	300
Bottlefed	500
Infants (7-12 months)	550
Young Children	
1-3 years	700
4-7 years	800
Boys	
8-11 years	800
12-15 years	1200
16-18 years	1000
Girls	
8-11 years	900
12-15 years	1000
16-18 years	800

Table 3: Proposed Physical Activity Recommendations for Australian Children and Youth

- All children and youth should be physically active daily, or nearly every day, as part of play, games, sport, work, transportation, recreation, physical education, or planned exercise, in the context of family, school and community activities.
- All children and youth should engage in physical activity of at least moderate intensity for 60 minutes or more on a daily basis
- Children and youth should avoid extended periods of inactivity thorugh participation in sedentary activities such as television watching, video, computer games and surfing the internet
- Children and youth who currently do little activity should participate in physical activity of at least moderate intensity for at least 30 min daily, building up to 60 minutes daily.

1.3.6 Calcium intake, physical activity and smoking premenopausal women

In common with children, there is substantial scope for improvement in osteoporosis preventive behaviours of calcium intake, physical activity and smoking in premenopausal women.

The current recommended dietary intake (RDI) for calcium in the US and Australia for women aged 25 –54 years is 800 mg but is variable across Europe with existing

guidelines generally recommending a daily intake of 700-800 mg [10]. Despite this information being widely available, low dietary calcium intakes have been reported frequently [105, 107-111]. In Australia, the National Nutrition Survey reported that over 50% of women aged 25-44 years did not meet the RDI for calcium and 25% of women in this age group had an intake of less that 554 mg/day or 70% of the RDI [105]. Other studies have shown similar low intakes in Australia [112] and in the United States [113]. The public health importance of this issue is widely recognized and increasing calcium intake has been targeted as part of nutrition policy in Europe, the US and Australia [10, 114, 115]. Australia has as a target that the proportion of people consuming diets with less than 70% of the RDI for calcium be reduced by half [115].

While there are recommendations for physical activity levels in adults for prevention of cardiovascular disease (adults should accumulate 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week) [116] and for cardiorespiratory fitness (participation in 3, 20 minute sessions of vigorous intensity physical activity per week) [117], similar guidelines specific to bone health are lacking. Nonetheless, even using these existing guidelines as a basis for comparison, it is clear that levels of physical activity in premenopausal women are low. The Australian Longitudinal Study on Women's Health [118] measured physical activity by questionnaire and classified women into active and inactive categories. In 1996 and 2000, over 40% of women aged 18 to 24 at baseline were classified as inactive (vigorous exercise less than 3 times per week or less vigorous exercise less than 5 times per week). At baseline in 1996, over 65% of women aged 45-50 years were also classified as inactive [119]. Other Australian studies have similarly reported low levels of physical activity (mean age 20 years) [120, 121], as have studies in the United States where 3 separate surveys found

that about 20-25% of women aged 18 to 44 did not take part in any leisure time physical activity and only around 15% and 20% undertook regular vigorous (3 sessions of >20 min at 50% of maximum cardio-respiratory capacity) or regular sustained (sustained activity for > 30 min > 5 times per week) physical activity [117]. In the UK General Household Survey of 2002, around 40% of women aged 25-44 had undertaken no sport or physical activity in the 4 weeks prior to being surveyed [122].

Smoking remains prevalent in young women in Australia but the prevalence has dropped from 30% in 1980 to 21% in 2001. In women aged less than 30, the prevalence was higher ranging from 28% in 18 to 24 year olds to 26% in 30-39 year olds in 2001. Furthermore, in 1995, only 42 to 48% of young women (depending on age group) had never smoked [123]. In the UK, 33% of women aged 25-34 and 27% of women aged 35-49 were smokers in 2002 [124].

1.3.7 Conclusion

Inadequate calcium intake and physical activity in children and premenopausal women and smoking in premenopausal women are common. Improving calcium intake and physical activity in childhood has potential benefits for prevention of fractures and of other diseases in childhood. Moreover, any improvements in diet or physical activity that begin in childhood and persist into adult life are likely to have extensive public health benefits in adult life. Similarly, changes to smoking, calcium intake and physical activity behaviours made in adult life may impact on osteoporosis, but are also likely to have wider public health benefits.

1.4 Changing osteoporosis preventive behaviours in premenopausal women

As discussed above, modifiable risk factors for low BMD include low calcium intake, low levels of physical activity and smoking [125]. Limited information is available currently on how to influence these osteoporosis preventive behaviours in premenopausal women. The approaches taken include educational interventions alone and educational interventions combined with bone density screening.

1.4.1 Educational interventions to change osteoporosis preventive behaviours

There are only a small number of controlled studies of educational interventions in pre-menopausal women aimed at improving osteoporosis preventive behaviours [126-129]. Two of these studies had interventions with a component including bone density screening but without any specific assessment of the effects of the bone density screening itself, separate to the overall intervention effect [127, 129].

One study examined the effects of brief written educational materials alone on calcium intake and physical activity [128] in 536 women (response rate low at 36%) aged 35-43 years identified from drivers license records in 3 North Carolina counties. There were four intervention groups, one receiving general information about osteoporosis, one receiving instructions on how to increase levels of exercise and calcium intake, one receiving both packets and a control group receiving no information. The withdrawal rate in this study was high, at 30%. No effects of information packets on calcium intake

or physical activity behaviours (measured by questionnaire) were observed in this study at either 1 month, 3 months or 12 months post-intervention.

The effects of a tailored educational intervention, either with or without an additional community intervention, on calcium intake and exercise level were studied in a convenience sample of 547 US women aged 40 to 56 [127] recruited from 12 North Carolina counties. The control (non-tailored intervention) consisted of two packets of information. The first contained general information on osteoporosis and specifically more detailed information on calcium and exercise requirements to reduce osteoporosis risk. The second packet provided tips on how to increase calcium intake and exercise levels. The tailored intervention contained the same information but with additional feedback appropriate to the participant's current levels of calcium and exercise, and participants also received a follow-up telephone counseling call targeting calcium intake and exercise levels. The community intervention was undertaken in 6/12 counties, and involved the establishment of an Osteoporosis Resource Centre with dissemination of educational materials; a workshop on osteoporosis and its prevention and bone density scanning performed on the study participants with results sent to them with their information packet. There was no attempt to measure any specific effect of the bone density screening on behaviours. Calcium intake and exercise level were measured by questionnaire at 3, 6 and 12 months. In women who did not meet their calcium requirements at baseline, the tailored materials did result in some short-term changes in calcium intake, but these did not persist at 12 months and there were no effects on exercise participation. The community intervention did not improve calcium or exercise behaviours.

Two studies examined the effectiveness of group education interventions to improve osteoporosis preventive behaviours. Peterson et al [129] studied a convenience sample of 122 premenopausal women aged 18 to 30 with low baseline calcium intake (<700 mg/day) as measured by questionnaire. The intervention group received 3 small group education sessions covering osteoporosis in general with review of participants' bone density results; ways of improving calcium intake; and reinforcing behaviour changes. At the second session subjects were also given a 6-month supply of calcium and vitamin D supplements to take. There was no description of how bone density results were presented, nor any specific assessment of the effects of results on behaviour changes. The control group received no intervention and received their bone density results only at the end of the trial. Eighty women completed the trial. Outcome factors were calcium intake and femoral, forearm and total body BMC measured at baseline, 3 months and 6 months. Not surprisingly, given that the intervention group was given calcium supplements to take, total calcium intake and supplemental calcium intake were both higher in the treatment group. However, there was no effect of the education intervention on dietary calcium intake. Change in total body BMC was also higher in the treatment group, but this may simply been due to the higher use of calcium supplements in this group. Brecher et al studied a convenience sample of 97 US women aged 25 to 75 years, of whom 23 were premenopausal. The treatment group received a single small group 3-hour educational session, the control group no intervention. Follow-up was over 3 months, with calcium intake measured by food frequency questionnaire and exercise activity measured by questionnaire being the behavioural outcomes measured. While after 3 months follow-up women in the treatment group did self-report that they had increased their calcium intake more frequently that the control group (83% vs. 58%), there were no objective differences in

calcium intake as actually measured, or in physical activity, between treatment and control groups. The results were similar regardless of age.

Overall, the evidence suggests that educational interventions alone have little effect on osteoporosis preventive behaviours. However, the studies described above are limited by their relatively short-term nature (maximum duration of follow-up 12 months); the lack of objective physical activity measures and the lack of any measures of the effects of behaviour change on BMD in all studies except Peterson et al [129]. The generalisability of the results of these studies is also open to question, due to selection biases and either high levels of withdrawals or systematic differences between subjects withdrawing and those completing the studies.

1.4.2 Bone density feedback as a behaviour changing tool

Three studies have specifically examined effect of BMD screening with feedback of results in combination with an information leaflet, on osteoporosis preventive behaviours after 12 months of follow-up [130-132].

Cook et al [130] recruited 771/2324 Caucasian women (33% response rate) aged 30 or more years, from 4 different medical practices, of whom about 1/3 were younger than 40 years. All respondents received an educational booklet about osteoporosis, which included information on dietary and lifestyle preventive measures and were offered a one hour educational workshop and free bone density screening by single photon absorptiometer. Of the 771 respondents, 32% attended the osteoporosis workshop and had bone density screening, 22% had bone density screening alone and the remainder

opted not to receive either. The screening appointment included explanation of results by a nurse. Dietary and physical activity changes were measured by self-report by questionnaire. At one year, 74.3% of the women who underwent screening reported behavioural changes, while only 53.8% of women who did not undergo screening reported changes. The changes were predominantly in diet and exercise, with low rates of change in smoking. A higher proportion of women with below normal bone mass reported change in diet and exercise than women with average or above bone mass (85.5% and 69% respectively for diet, $p<0.001$; 53.6% and 39.6% for exercise, $p<0.01$). Changes in smoking behaviour were also more often reported in women with low bone mass (6.4% compared to 3%) but this was not statistically significant. In unscreened women who did not attend a workshop, 53.8% of women reported lifestyle changes at one year, with 49% reporting diet changes, 21% reporting exercise change and 2% reporting changes in smoking, which was less than that observed in groups who received bone density screening regardless of bone density result.

Jones and Scott [132] provided bone density feedback to a convenience sample of 271 premenopausal women (mean age 33 years), combined with an osteoporosis information leaflet. The result were that those with low BMD (defined as BMD of < -1.0 at the femoral neck of lumbar spine) had higher self-reported rates of increased calcium intake (61% vs 9%), calcium supplement use (39 vs 4%) and increased physical activity (41 vs 17%) (all $p<0.001$). Self-reported smoking cessation rates were similar in both groups (16 vs 17%, $p=0.93$). Calcium intakes in the low BMD groups, as measured by food frequency questionnaire, were higher after the intervention (1172 vs 915 mg/day, $p<0.001$), but no there were no significant changes in physical activity levels measured by questionnaire.

The findings of Jones were confirmed by Jamal et al [131] in an intervention study of bone density feedback and tailored written information packs in a convenience sample of 669 healthy premenopausal women (mean age 27.5 years). Lifestyle behaviours compared pre and post intervention were: smoking; drinking at least one alcoholic beverage per day; drinking at least one glass of milk per day; drinking 3 or more caffeinated beverages per day; using the oral contraceptive pill; walking (<1/4 km per week, ¼ to 3 km/week, 3 to < 6 km/wk and 6km or more /week); and use of calcium and vitamin D supplements. In this study, women who had low BMD were more likely to use calcium supplements (OR 1.7, 95%CI 1.2-2.3) and vitamin D supplements (OR 1.6, 95%CI 1.1-2.2) but there were no significant differences in the other behaviours measured.

A fourth study [133] examined the impact of pharmacist-led BMD screening together with a risk factor assessment and personalized counseling on behaviour change measured by self-report at 6 months in a convenience sample of 102 women (median age 57 years, range 26-93 years). No specific assessment was made of effects in premenopausal women alone. There was no control group, nor any comparison between changes made in low vs. high BMD individuals and the independent effects of the feedback of scan results compared to the effects of the questionnaire risk assessment and counseling were not ascertained. The results suggested that the screening process overall may have had an effect, with 43% of participants reporting increasing their dietary calcium intake, 29% using calcium supplementation and 55% modifying smoking status, exercise, alcohol consumption or caffeine intake.

The studies above have significant limitations. All studies were limited to one year or less of follow-up and none measured BMD as an outcome. The limitations of the study

by Summers et al are discussed above. The study by Cook et al [130] was limited by its poor response rate (33%) and high loss to follow-up (33%) as well as by the interventions not being randomised. In the study by Jones and Scott [132], there was limited baseline data on behaviours available so that changes in behaviour could not be assessed. The sampling methods used in Jamal et al [131] were likely to lead to bias eg healthy cohort effect. While this study measured outcomes both before after intervention, the study showed differences in calcium and vitamin D supplement use only. However, the assessment of walking by self-report used in this study has not been validated.

While the evidence from these studies supports the suggestion that bone density feedback may improve osteoporosis preventive behaviours, the limitations of the previously described studies means that further research into the efficacy and effectiveness of bone density feedback as a means of promoting changes in osteoporosis preventive behaviours is needed. Specifically, what is needed is a test of the effectiveness of bone density feedback in a random, population-based sample of premenopausal women, with:

- objective measures of behaviour change,
- measures taken over a longer period of follow-up,
- and, with measurement of BMD outcomes.

1.5 Changing osteoporosis preventive behaviours in children

Strategies to maximize peak bone mass in girls and boys have been identified as a priority area for research [125]. However, information on how to specifically improve

osteoporosis preventive behaviours by lifestyle interventions in children, particularly in healthy children, is sparse.

One randomised controlled trial examined the effects of a lifestyle intervention aimed at improving diet (increasing the consumption of fruits, vegetables and high calcium foods; and moderating sodium and soft drink consumption) and increasing physical activity that involves high impact and spinal motion in adolescent females (aged 14-16 years) [134]. The intervention was intensive, including group and individual components, with an overnight retreat, annual individual visits, quarterly phone coaching, bimonthly team meetings and weekly self-monitoring postcards. Diet and physical activity were assessed by a 24-hour and 72-hour recall respectively. Interim results from 1 year of follow-up from this trial (full results are not yet published) showed increases in calcium intake and fruit and vegetable intake, decreased soft drink intake but no changes in physical activity [135].

Another two year, community-based, group-randomised trial [136] aimed to promote bone mass gains among 9-11 year old girls through an intervention consisting of an intensive series of ten 90-minute activity-based sessions based on Social Cognitive Theory, focusing on the development of behavioural skills to choose calcium rich foods and engage in weight-bearing physical activity. Calcium intake was measured by 24 hour recall and physical activity by questionnaire (the physical activity checklist Interview). In this study, calcium intake increased, with a treatment effect of 92 mg/day at two years, but there was no change in weight-bearing physical activity.

The lack of success in these two preceding studies at improving levels of physical activity is not entirely unexpected. Two recent reviews of studies of interventions to promote physical activity in children and adolescents [137, 138] reported that even quite complex interventions based on interventions both within and outside schools did not necessarily result in improved levels of physical activity. It is clear that altering physical activity behaviours may be more difficult than altering diet in children.

There have been two randomised controlled trials in children with inflammatory bowel disease [139] and with juvenile rheumatoid arthritis [140] which compared two methods of increasing dietary calcium intake. Both of these diseases place children at increased risk of low bone mass. The first intervention was a behavioural intervention consisting of 6 sessions over 8 weeks. Parents and children were seen separately. Parents were provided with nutrition information about high calcium food choices, and received training in child behaviour management strategies. They kept a diary of their children's meals and at each session received graphical feedback on their children's average calcium content of each meal. Individualised advice was also given. The children received age-appropriate, entertaining educational activities concerning calcium and bone health. The control intervention was an approximation of the dietary counseling that would routinely be given, with the same nutrition information being given as in the behavioural intervention. There were 3 sessions over 8 weeks. In children with inflammatory bowel disease, the behavioural intervention was shown to be more effective at increasing calcium intake (increase of 984 mg/day c.f to 274 mg/day in the control group [139]. Similar results were reported in the study of children with juvenile rheumatoid arthritis [140]. Both of these studies report only short-term results (post the 8 week intervention) and whether these improvements will be maintained in the longer

term is not yet known. It is also unclear whether these interventions would be as effective in healthy children i.e. in children without diseases predisposing them to low bone mass.

Changing lifestyle factors in children has been more often addressed in the context of the prevention and management of obesity. As in osteoporosis prevention, strategies for obesity prevention and treatment in children also involve dietary and physical activity changes. While there is a greater literature examining this area, the studies are heterogeneous, and often in small and highly selected populations, so the types of interventions that are most effective remain unclear [141]. There is limited RCT evidence to demonstrate the efficacy of influencing children's behaviour by intervening with parents alone but this suggests that using parents as exclusive agents of change is more effective at reducing weight in children than intervening directly with children [142] and that the improvement persists over time [143]. There is, however, observational evidence suggesting that this approach is worthy of further exploration [144-147]. Therefore, while there is little research addressed at altering osteoporosis preventive behaviour in children, the data described examining lifestyle behaviour change for obesity indicates that intervening directly with parents has potential to be effective.

1.6 Osteoporosis knowledge and self-efficacy

There are a number of models that have been used to examine lifestyle behaviour change. Two key factors involved in lifestyle change related to osteoporosis prevention are osteoporosis knowledge and the concept of self-efficacy.

1.6.1 Osteoporosis Knowledge in Women

There is evidence suggesting that osteoporosis knowledge is one contributor to osteoporosis preventive behaviour, though this is not a clear-cut relationship. Cross-sectional studies have varied in whether they found an association between levels of osteoporosis knowledge and osteoporosis preventive behaviours [148-152] with a clear association being found in only one case [152]. Another cross-sectional study utilizing the precaution adoption process model found that women who were in the never-engaged stage of change (ie unaware of the health problem and of the precaution recommended to reduce the risk of experiencing the problem) had the lowest levels of osteoporosis knowledge and that knowledge levels tended to be higher in women at higher stages of change [153].

Prospective studies similarly have been conflicting with some studies demonstrating increases in osteoporosis knowledge and concurrent improvements in osteoporosis preventive behaviours [126, 130, 154] but others demonstrating changes in knowledge but not behaviour [128, 155]. In one prospective study, causal analysis was used to demonstrate that osteoporosis knowledge was an important contributor to exercise and calcium intake behaviour [156]. Measurement of osteoporosis knowledge is itself problematic and variations in the approach taken to measuring osteoporosis knowledge may be part of the reason for the variation in the results of the studies described previously. There are three partially or fully validated instruments to measure osteoporosis knowledge described in the literature [157-159]. In the studies described, only three used one of these questionnaires [151, 155 156].

Most studies of osteoporosis knowledge levels have been in highly selected populations or have not used validated instruments to measure osteoporosis knowledge but the results have almost uniformly demonstrated low levels of knowledge [130, 149, 151, 154, 155, 160-163]. One exception was a study in 16-59 year old Norwegian women showed higher knowledge levels with women scoring a mean of 78% of the maximum score in using an instrument that was not validated [164]. Two other studies which reported unusually high levels of knowledge were convenience samples of college students enrolled in a basic health course [148] and in nursing [165], where selection bias was likely to have played a role in the results.

Few studies have reported levels of osteoporosis knowledge in random, population-based samples [128, 164, 166, 167] and all have demonstrated low levels of knowledge. None of these studies used validated instruments to measure osteoporosis knowledge and information available about the psychometric properties of the tools used was limited. None have specifically examined knowledge in premenopausal women in the 25-44 year age range. Therefore, while the evidence suggests that osteoporosis levels are in general low in women at a population level, studies measuring standardized osteoporosis knowledge levels in the general population and specifically in premenopausal women are lacking.

1.6.2 Osteoporosis Self-efficacy

Self-efficacy refers to "people's judgments of their capabilities to organize and execute courses of action required to attain designated types of performance" [168]. Osteoporosis self-efficacy specifically assesses people's confidence in being able to change

osteoporosis preventive behaviours related to calcium intake and physical activity. As discussed by Horan [169], Bandura relates self-efficacy to behaviour in three ways: the conviction that one has the ability to (a) initiate the activity, (b) maintain the activity and (c) persist in performing the activity in the face of obstacles. Bandura [168, 170]describes four main influences on self-efficacy. These are:

1. Mastery experiences. This refers to a person's actual experience of accomplishing the behaviour. Succeeding in a behaviour helps build belief in one's personal efficacy, particularly successes achieved after overcoming obstacles.
2. Vicarious experiences (or modeling). The vicarious experiences provided by social models also affect self-efficacy. "Seeing people similar to oneself succeed by sustained effort raises observers' beliefs that they too possess the capabilities master comparable activities to succeed." [170]Competent models also transmit knowledge and teach observers effective skills and strategies to succeed in a behaviour.
3. Social persuasion. Others can persuade people that they are capable of accomplishing a particular behaviour and conversely persuade people that they are not.
4. Somatic and emotional states. This refers to the effects of a person's physical and emotional reactions, and the person's perception of these reactions on self-efficacy. For example, physical symptoms of stress may be interpreted negatively and reduce self-efficacy. Mood also affects people's judgments of their personal efficacy. Positive mood enhances perceived self-efficacy and vice versa.

Self-efficacy has been studied in the setting of numerous diseases and behaviours. It has been described as potentially one of the most important and modifiable predictors of

physical activity [171] and has been reported as the strongest predictor of a health-promoting lifestyle [172]. The concept of self-efficacy underpins the concept of chronic disease self-management, as originally developed for use in arthritis self-management [173, 174]. In this context, group education based on self-efficacy concepts has been shown to be modestly effective in symptomatic populations at reducing health care utilisation and improving health status [173, 174]. Osteoporosis self-efficacy has been demonstrated to be an important determinant of exercise and calcium intake behaviours relevant to the prevention of osteoporosis [153, 156].

A validated instrument to measure osteoporosis self-efficacy was developed by Horan et al [169] and is described more fully in the methods of this thesis (see Chapter 3). This instrument measures two subscales: calcium self-efficacy and exercise self-efficacy. Few studies have measured osteoporosis self-efficacy levels in young women [126, 151, 162, 165, 175]. The scoring of the osteoporosis self-efficacy scale have varied between these studies, so the results of the different studies that follow are reported as a percentage of the maximum possible score for comparison purposes.

Moderate levels of both exercise and calcium self-efficacy (scores of 63 % and 68% respectively) were found in a random sample of female undergraduates college students (age range 17-64, mean age 28 years) in the United States [151]. The response rate of this study was very low (28%) so there was a high risk of selection bias in this study. Similar levels were reported in one small sample of US nursing students (n=31, age 18-21 years) with exercise and calcium subscale scores being 74% and 75% respectively [175]and again in a larger sample (n=194) of similar students with exercise and calcium subscale scores being 65% and 71% respectively [165]. In a survey of similarly aged

sample of Thai nursing students mean exercise self-efficacy was 53% and calcium self-efficacy 66% [162]. Lower levels of overall osteoporosis self-efficacy (score 41% of maximum) were found in a convenience sample of 25-75 year old US women [126] recruited as volunteers via newspaper advertisements, posted notices, mailings and word of mouth. Given the populations in which the higher levels of self-efficacy were measured, it is likely that in the general population levels may well be at the lower level, but as for osteoporosis knowledge, a random population-based sample with an adequate response rate is needed to properly determine osteoporosis self-efficacy levels in premenopausal women.

1.6.3 Changing Osteoporosis Knowledge and Osteoporosis Self-efficacy

As discussed above, both osteoporosis knowledge and self-efficacy appear to be contributors to osteoporosis preventive behaviours. Despite this and the available literature suggesting that both osteoporosis knowledge and osteoporosis self-efficacy are low in premenopausal women, there is limited information about how best to improve osteoporosis knowledge and osteoporosis self-efficacy at a population level.

Three randomised controlled trials (RCT) of similar single-session osteoporosis education programs conducted in Thai nursing students [162], in students in a US pre-nursing course [175] and in self-selected US women aged 25-75 [126] have all demonstrated increases in short-term (range of follow-up 2 weeks to 3 months) osteoporosis knowledge but only one study [162] demonstrated an increase in osteoporosis self-efficacy. In a population-based sample, a RCT of three forms of mailed-out osteoporosis educational material vs. no material [128] was performed as described previously in

Chapter1.4.1. A general osteoporosis information packet increased short-term knowledge levels (at 3 months) but the increase did not persist at 12 months. One uncontrolled study used an information booklet with patients self-selecting for bone mineral density measurement with discussion of results by a nurse, and/or a one-hour osteoporosis education workshop [130]. This study suggested that the information leaflet was as effective at increasing knowledge as the 1-hour workshop, and that bone density screening also increased knowledge levels. Data from uncontrolled studies [131, 132] has suggested the feedback of BMD to premenopausal women may also be effective at changing osteoporosis prevention behaviours at 1 year. There is no published data demonstrating the effect of individualised BMD feedback on levels of osteoporosis knowledge or osteoporosis self-efficacy levels. Furthermore, it is not known whether BMD feedback and educational interventions produce independent effects on osteoporosis knowledge and osteoporosis self-efficacy.

Chapter 2: Research Questions

Osteoporosis is a major and growing public health problem, particularly in women [2, 3] and is a significant public health problem both in Australia and internationally. Low bone mineral density (BMD) is a major risk factor for osteoporotic fracture [39]. BMD in later life is a function of peak bone mass and the rate of subsequent bone loss [30]. Although bone mineral density is lost most rapidly post-menopausally, it has also been shown that premenopausal women have significant age-related BMD loss [19-21] and that premenopausal bone mass contributes to fracture risk in later life [31].

Modifiable risk factors for low BMD include low calcium intake, smoking and low levels of physical activity [125] and as discussed in Chapter 1.3.6 there is substantial scope for reducing the currently high prevalence of inadequate calcium intake, inadequate physical activity and smoking in premenopausal women. However, limited information is available currently on how to influence these risk factors in premenopausal women. As discussed in Chapter 1.4.2 there are studies suggesting that BMD screening with feedback of results combined with an information leaflet can improve self-reported osteoporosis preventive behaviours in premenopausal women after 12 months of follow-up. In particular, greater changes in behaviour were reported in women with low BMD. However, there have been no longer-term follow-up studies or studies of the effect, if any, of these behaviour changes on BMD. Studies of educational interventions in pre-menopausal women that have not included a bone density feedback component [126-128, 155] have also been short-term and have not studied effects of behaviour change on BMD. Similarly to premenopausal women, in children calcium intake and physical activity levels need to be improved (see Chapter 1.3.5), and yet there have been few studies examining ways to accomplish this (see Chapter 1.5).

The aim of this thesis was to examine potential ways to improve calcium intake, physical activity and bone mineral density in women and in children. The main part of this thesis describes a study of the effects of individualised bone mineral density (BMD) feedback and two different educational interventions (group-based behavioural education and an osteoporosis information leaflet) on osteoporosis preventive behaviour and 2-year change in BMD in pre-menopausal women.

Specifically, with this study we aimed to test the following à priori hypotheses:

1. Women are more likely to change calcium intake and physical activity if their BMD is low.
2. Group education (in the form of the Osteoporosis Prevention and Self Management course) will be more efficacious at changing these lifestyle behaviours than an information leaflet alone.
3. Bone density feedback and educational intervention have independent effects on behaviour and BMD change.
4. Women who improve their physical activity or dietary calcium intake will have a change in bone mass over 2 years that is 0.34-0.54% per annum better (depending on site and lifestyle factor) than those who do not alter their behaviour.

Secondary aims of this study are described more fully in the relevant chapters. In brief they were:

1. to describe the cross-sectional association between socio-demographic factors and calcium intake, and to evaluate the association between having

low milk intake and meeting the RDI for calcium, in a representative sample of healthy women aged 25 to 44 years. (See Chapter 5).

2. to compare the effects of BMD feedback and two educational interventions, group-based behavioural education and an osteoporosis information leaflet, on short and longer-term changes in osteoporosis knowledge and osteoporosis self-efficacy in women aged 25-44 years (see Chapter 6).
3. to assess whether these same interventions administered to mothers have potential to influence children's behaviour, by comparing their effects on maternal-report of children's behaviour change (see Chapter 8).

The second study in the thesis is a qualitative study exploring further the findings described in Chapter 8 and this qualitative study is described in Chapter 9. A third study is a systematic review of the effects of calcium supplementation in children on bone mineral density, described in Chapter 10. The full details of the background and objectives of both these additional studies are given in the relevant chapters.

Chapter 3: Methods

The study was performed in Southern Tasmania in 2000-2003. The population of the region is predominantly Caucasian and as at June 1999 numbered 194 389 with 28 839 women aged between 25 and 44 years of age [176]. Subjects were selected at random in this age range with equal probabilities of selection using the year 2000 Tasmanian Electoral Roll as the sampling frame. Voting is compulsory in Australia and this register of electors provides a comprehensive population listing that is estimated to be 95% complete for persons of these ages [177]. Recruitment was by letter, followed up if necessary by phone contact. Subjects were excluded if they had previously had measurement of bone densitometry, had thyroid disease, renal failure, malignancy or rheumatoid arthritis, had a history of hysterectomy, were on hormone replacement therapy or were pregnant or planning pregnancy within 2 years of study entry, or were lactating. A total of 146 subjects were excluded on these grounds. Ethics approval was obtained from the Royal Hobart Hospital Ethics Committee and all subjects gave written informed consent.

Interventions

All participants received individualised bone density feedback as described below. Before their BMD result was known, all subjects were randomised to receive in addition one of two educational interventions: an information leaflet produced by Osteoporosis Australia "Understanding Osteoporosis"; or the Osteoporosis Prevention and Self-management Course (OPSMC). Prior to recruitment, a random number drawn from a (0,1) uniform distribution (using the random number generator in SAS) was allocated to a participant number (which were consecutive integer values starting at 1). The

random numbers were rounded to 0 if less than 0.5, or 1 if greater than or equal to 0.5. The 0 or 1 produced the assignment to one of the two educational intervention groups. Participants were allocated a participant number on recruitment. While there was no allocation concealment, allocations were implemented sequentially for each participant number with no variations to the order in which the numbers were assigned, to minimise the potential for bias.

Bone density feedback

Subjects had their bone mineral density at the spine and hip, together with body composition, measured at baseline and at 2 years (Hologic QDR2000, Waltham, MA). At baseline, those with a mean T-score at spine and hip of greater than or equal to 0 received a letter informing them that they were not at a higher risk of fracture in later life, whereas those who had a mean T-score of less than 0 were informed that they were at higher risk. This was based on the observation that those in the lower half of the BMD distribution have threefold higher fracture risk both in later life and in the early postmenopausal period [38] suggesting that bone density tracks throughout life as has been recorded in children [178]. Though this cut off is based on women older than in the current study, there is evidence that has led to the proposition that bone mass tracks throughout life [41] so that women who are in the lower BMD range premenopausally may go on to have lower BMD postmenopausally. T-scores were used rather than Z-score as the emphasis of the individual feedback was on fracture risk in later life, as predicted by T-scores, rather than current fracture risk. However, given the young age of our sample, the distribution of Z-scores and T-scores was very similar.

Education

The OPSMC is a chronic disease self-management course based on the work of Lorig [173, 174] developed by the Arthritis Foundation of Victoria and utilized by Osteoporosis Australia. This small group patient education program aims to increase knowledge, improve confidence and awareness and self-management of osteoporosis prevention with an emphasis on promoting appropriate lifestyle change such as increasing calcium intake, increasing appropriate physical activity and smoking cessation. Behavioural and educational methods include lectures, discussion, brainstorming, demonstration and small group work. The OPSMC had a maximum of 16 subjects per group and were held at regular intervals for 2 hours per week for four weeks and were delivered by 2 of 12 Department of Health and Human Services allied health professionals (physiotherapists, occupational therapists and nurses). Participants randomised to the leaflet intervention received the same osteoporosis information leaflet as in our previous study [132]. The leaflet provides a description of osteoporosis, an overview of the role of lifestyle factors such as diet, exercise and smoking and outlines ideal levels of calcium intake and exercise. It was considered unethical to provide no educational information to subjects so the leaflet was given as minimal information. Participants randomised to the leaflet intervention received their BMD feedback with the leaflet and participants randomised to the OPSMC received their BMD feedback at the first session of the course.

The combination of individualised bone density feedback providing different fracture risk feedback according to T-score, with randomisation to leaflet or OPSMC educational intervention resulted in four groups each with a different combination of

interventions. These were: Group 1 = Randomised to leaflet with T-score 0 or above who received feedback of not being at increased risk of fracture in later life; Group 2 = Randomised to OPSMC with T-score 0 or above who received feedback of not being at increased risk of fracture in later life; Group 3 = Randomised to leaflet with T-score < 0 who received feedback of being at higher risk of fracture in later life; Group 4 = Randomised to OPSMC with T-score < 0 who received feedback of being at higher risk of fracture in later life.

Outcome Measures

Primary Outcome Measures

(1) Bone mineral density at the femoral neck and lumbar spine

This was measured by Hologic QDR2000 densitometer on fan beam setting at baseline and 2 years. Reproducibility in adults is of the order of 2-3% [38].

(2) Calcium intake

Usual calcium intake was assessed at yearly intervals by a short food frequency questionnaire (FFQ) designed specifically to measure calcium intake, with a reference period of the last 12 months (see Appendix 1). The FFQ has been validated in Caucasian Australian women against 4 day weighed dietary records. The correlation between methods for estimated calcium intake was high ($r = 0.79$, $p=0.001$) [179]. Calcium content of food categories was assigned using Australian food composition tables [180], and usual calcium intake estimated in mg/day. Information on whether respondents were taking calcium supplements was also obtained by questionnaire. Respondents were classified as taking calcium supplements if they reported taking a supplement

containing calcium alone or as a main ingredient, and at a frequency of not less than 4 times per week.

(3) Physical activity

Energy expenditure and sports participation was assessed annually by a questionnaire validated in US adolescents[181] which has been modified for Tasmanian conditions and used previously in women in this age group where it was associated with bone mass at the femoral neck [61] (see Appendix 2). In this questionnaire, strenuous physical activity levels were assessed by how many days in the last 14 the subjects reported performing at least 20 minutes of strenuous exercise and light exercise , measured in five categories (1 = 0 days, 2 =1-2 days, 3 = 3-5 days , 4 = 6-8 days, 5 = 9 or more days).

(4) Fitness

Muscle strength and endurance fitness was assessed at baseline and two years. Muscle strength was assessed by dynamometry in the lower limb. The intraclass correlation coefficient for lower limb strength was 0.88 (95% CI 0.84, 0.92) at baseline and 0.82 (95% CI 0.73, 0.92) at 2 years. Endurance fitness was assessed by bicycle ergometer where physical work capacity at 170 beats per minute was estimated by progressively increasing sub maximal workloads [182]. This measure correlates well with treadmill assessment of VO_2max [183].

Secondary Outcome Measures

(1) Osteoporosis knowledge

This was measured by the Osteoporosis Knowledge Assessment Tool (OKAT), a survey instrument based on the common content of the OPSMC and the leaflet "Understanding Osteoporosis" (see Appendix 3). The OKAT has 20 items, each having true, false and

don't know options. Scoring was 1 for a correct response and 0 for an incorrect or don't know response. The possible range of scores was 0 to 20. The questionnaire had a Ferguson's sigma of 0.96, a Cronbach's alpha of 0.70 and factor analysis consistent with only one factor (osteoporosis knowledge) being measured. Complete details of the psychometric properties of the OKAT are described in Chapter 4. Osteoporosis knowledge was measured at baseline, 6 weeks and 2 years.

(2) Osteoporosis self-efficacy

Osteoporosis self-efficacy was measured by the osteoporosis self-efficacy scale (OSES) [169] and has 6 items in each of two subscales, one relating to calcium intake and one relating to physical activity. We used a four point adjectival scale modification of the original scale, with ratings of: not at all confident (score 1), mildly confident (2), confident (3) and very confident (4) (see Appendix 4). The range of possible scores was from 12 to 48. Osteoporosis self-efficacy was measured at baseline, 1 year and 2 years.

(3) Maternal report of changing their children's calcium intake and/or physical activity

After 1 year of follow-up, subjects were asked for *yes/no* responses to the questions: "If you have children, have you changed their: Calcium intake? Physical activity?" After 2 years, they were asked: "If you have children, in the last year have you changed their: Calcium intake? Physical activity?" with options of increased, decreased or same (see Appendix 5).

Other factors measured at baseline and 2 years were: height by stadiometer (The Leicester height measure, Invicta Plastics Ltd, Oadby, England) and weight by a single

set of calibrated scales (Heine, Dover NH USA). Body mass index was calculated (kg/m^2). Questionnaire assessment was made of smoking history (current/former/never, cigarettes per day, age at uptake, age at ceasing), breastfeeding history (ever breastfed, time since last breastfeeding), number of children, family history of osteoporosis and/or fracture, as well as fracture history in the subject, education level (4 point scale: less than grade 10, up to grade 10, completed grade12, tertiary), employment status of main financial provider in the household (employed or unemployed), hours of employment of the respondent (0, less than or equal to 20 or >20 hours per week) and marital status (see Appendix 6). Stage of change was measured by questionnaire (see Appendix 4) for both calcium and physical activity behaviours, based on the Transtheoretical Model of behaviour change which identifies 5 motivational stages, namely precontemplation, contemplation, preparation, action and maintenance [184].

At one and two years, subjects were followed up by mail, using the questionnaires described above, and by asking a series of yes/no questions to assess self-reported change in smoking, dietary calcium intake, calcium supplement use and physical activity.

As the subjects were aware of both their BMD status and of the intervention they received, blinding of assessors was not attempted.

The full study sample was used for the cross-sectional analysis (Chapter 5) and the randomised controlled trial reported in Chapters 6 and 7. Data from mothers only was used for the sub-study examining effects of the interventions on maternal report of

behavioural change in children (Chapter 8), and small sample of these mothers were interviewed for the study reported in Chapter 9.

Statistical Analysis

All statistical analyses were based on the à priori hypotheses described in Chapter 2. We performed statistical power calculations, which indicated that we had power of 0.8 ($\alpha = 0.05$ (two-tailed)) to detect clinically meaningful changes in calcium intake and physical activity, and differences in BMD of 1% per annum or better. Other statistical methods for each analysis are described in the relevant chapters. Detailed description of sample size calculations are given below.

Sample Size Calculations

The à priori hypotheses for which sample size calculation were performed are given in Chapter 2. Assuming $\alpha = 0.05$ (two-tailed), $\alpha = 0.2$, that the findings of Jones and Scott [132] apply, that the rate of change in the whole population is 0% pa and that the SD of the rate of change at the femoral neck and lumbar spine is the same as in an Australian longitudinal study in the elderly [185] then a total sample size of 400 had the power to detect the following effects shown in Table 4:

Table 4: Sample size calculations

	Baseline[1]	Hypotheses 1,2	Observed % changing[2]	Hypothesis 4
Smoking	42%	13% stop	6% stop[3]	0.66-1.00%pa
Adequate calcium intake	40%	14% increase	35% overall increase intake	0.34-0.50%pa

Sports participation	30%	13% increase	29% overall increase activity	0.35-0.54%pa

[1]actual data from Jones and Scott [61], [2]from Jones and Scott [132]; [3]data for smokers is % of all women who stop not smokers alone.

As seen in Table 4, the proposed sample size has adequate power to detect changes in calcium intake and physical activity of smaller magnitude than those previously observed with bone density feedback [61] but has less power to detect changes in smoking. For hypothesis 3, we assume that bone density feedback and education are additive i.e. the subgroup who has low bone density and receives the small group program will have 26-28% change in lifestyle factors as compared to those with normal bone density who receive the information leaflet. From the table it can be seen that there is also good power to detect small changes in bone mass with all three lifestyle factors over a two year follow up period.

Chapter 4: The design of a valid and reliable questionnaire to measure osteoporosis knowledge in women: the Osteoporosis Knowledge Assessment Tool (OKAT).

4.1 Introduction

Osteoporosis is a major and growing public health problem in both sexes but particularly in women [2, 3]. Physical activity and adequate calcium intake are both important for the prevention of osteoporosis [125]. There is evidence suggesting that osteoporosis knowledge is a contributor to osteoporosis preventive behaviour, though this is not a clear-cut relationship as discussed in detail in Chapter 1.6.1. Few studies have reported levels of osteoporosis knowledge in random, population-based samples [128, 164, 166, 167]. While for the most part these suggest that levels of osteoporosis knowledge are low (with one exception [164]), none of these have utilized validated instruments to measure osteoporosis knowledge and information available about the psychometric properties of the tools used is limited. None of these studies have specifically examined knowledge in women in the 25-44 year age range. Therefore, standardised osteoporosis knowledge levels in the general population and specifically in the 25-44 year age range remain unclear.

Measurement of osteoporosis knowledge is itself problematic and this may be part of the reason for the variation in the results of the studies described previously. There are three partially or fully validated instruments in the literature to measure osteoporosis knowledge [157-159]. We required an instrument in which all items were relevant to the Australian population. For example, two items in the Facts on Osteoporosis Quiz [157] referred to comparisons to African-American women, which were not relevant to populations outside the USA. The planned use of the instrument was to study women who had reached peak bone mass, but were premenopausal, so the instrument needed to have been fully validated in the 25-44 year age range. As the instrument was to be

administered as part of a large study, it had to be suitable for self-administration, and easy to code the results. None of the existing instruments satisfied all these criteria.

The aim of this study was therefore to describe the development of and psychometric properties of an instrument to measure osteoporosis knowledge for use in a population-based random sample of 25-44 year old women.

4.2 Methods

The study was carried out in Southern Tasmania, Australia as part of an ongoing study examining the effects of lifestyle factors on bone mineral density in women aged 25-44 years. A full description of the overall study design and methods is given in Chapter 3.

Osteoporosis knowledge was measured in subjects at baseline from April to November 2000. The survey instrument was based on knowledge content common to the Osteoporosis Prevention and Self-management course (OPSMC) and an information leaflet produced by Osteoporosis Australia "Understanding Osteoporosis". The OPSMC is a chronic disease self-management course developed by the Arthritis Foundation of Victoria and utilized by Osteoporosis Australia. Osteoporosis Australia is the peak body involved in community-based osteoporosis education in Australia. The OPSMC is a small group education program that aims to increase knowledge, improve confidence and awareness and self-management of osteoporosis prevention with an emphasis on promoting appropriate lifestyle change. Educational methods include lectures, discussion, brainstorming, demonstration and small group work. The information leaflet covers information on osteoporosis including its definition, natural

history of bone strength, risk factors and preventive behaviours, including physical activity and calcium intake.

The items were selected from the common material in the two interventions by a consultant rheumatologist and researcher who has specialist expertise in osteoporosis. The knowledge instrument aimed to measure a broad range of osteoporosis knowledge items that would be applicable to the Australian and to avoid items that would be difficult to adapt to other settings in which osteoporosis demographics might be different. It is a 20-item questionnaire, with each item having true, false and don't know options (see Appendix 3). The analysis was performed by scoring 1 for a correct response and 0 for an incorrect or don't know response. The total score could range from 0 to 20. Face validity was also assessed using a panel of 20 people from our institution. These included research nurses, research assistants and administrative staff.

Other factors measured in the protocol are described in Chapters 3.

Statistics

The psychometric properties of the osteoporosis knowledge questionnaire were assessed by examining:

1. The Flesch reading ease. This assesses readability based on the average number of syllables per word and the average number of words per sentence. Scores range from 0 to 100. Standard writing averages approximately 60 to 70 [186]. The higher the score, the greater the number of people who can readily understand the document.

2. The index of difficulty. This is defined as the proportion of patients answering the item correctly and is calculated by: number of correct responses/total number of responses [187]. An item with an index of difficulty higher than 0.75 is deemed to be poor, as it is too frequently answered correctly.
3. Item discrimination [187]. This tests how well an item discriminates between people who have a low and high osteoporosis knowledge score. For each item, a D-value is calculated by subtracting for each item the proportion of respondents answering correctly in the lowest quartile from those answering correctly in the highest quartile, aiming for a mean D-value of 50%.
4. Discriminatory power measured by Ferguson's sigma. This has a minimum of 0 if all subjects get the same score, and a maximum of 1 if the subjects are equally divided among all possible scores as is desirable.
5. Inter-item correlation matrix. This was performed to check for negative correlations and to screen for items with consistently weak correlations with other items ($r<0.09$, based on a sample size of 467, and $p> 0.10$).
6. Item-total correlations. The correlation of an item with the remainder of the scale with that item omitted is the item-total correlation. A correlation of <0.20 is considered poor [188].
7. Cronbach's alpha. This is a measure of inter-item consistency, and ranges from 0.0 to 1.0. If omitting an item increases Cronbach's alpha significantly, then excluding the item increases the homogeneity of the scale, which is desirable.
8. Factor analysis. Principal components factor analysis ascertains whether if the underlying factors identified statistically within data collected by a

survey instrument are consistent with the theoretical factors one was aiming to measure with the instrument. It also assesses whether the loading of individual items on the identified factors are consistent with the premise on which the survey instrument was constructed, though in the case of dichotomous items, these loadings need to be interpreted with caution [189]. In the case of questionnaires assessing knowledge, avoiding dichotomous items is problematic. Factor analysis has been used before in this context [159]. In this study, we would expect only one main factor (namely osteoporosis knowledge) with items loading above 0.3 [190] on this factor.

All analyses were performed in Stata version 7 (Stata Corporation, Texas, USA), except for the Flesch reading ease which was calculated in Microsoft Word 2000(Microsoft Corporation). A p-value< 0.05 (two tailed) was regarded as statistically significant.

4.3 Results

A total of 467 women were recruited (response rate 53%). The characteristics of subjects are given in Table 5. Due to small numbers in the lowest educational level and in some categories of marital status, these data are presented as three categories of education and two of marital status (married or defacto and other). The average age of participants was 37.8 years, and there was a wide spread of participants across educational levels and levels of employment. The average baseline osteoporosis knowledge score was 8.8 out of a possible 20 (s.d 3.3, range1 to 17).

Table 6 gives psychometric characteristics of the OKAT. The questionnaire had a Flesch reading ease of 45. If the word osteoporosis were removed from the questions or substituted with the term "thin bones", the reading ease rose to 65 and 68, respectively.

The index of difficulty for most items was satisfactory (between 0.12 and 0.66). Items 1 (*Osteoporosis leads to an increased risk of bone fractures.*), 4 (*Osteoporosis is more common in men.*) and 10 (*Any type of physical activity is beneficial for osteoporosis.*) scored above 0.75, indicating that most subjects answered these questions correctly.

The mean D-value for the questionnaire was 44%. Ferguson's sigma for the questionnaire is 0.96 which is very high.

There were no negative inter-item correlations. Items 9 (*From age 50, most women can expect at least one fracture before they die.*), 7 (*A fall is just as important as low bone strength in causing fractures.*) and 10 performed poorly when inter-item correlations were examined. These items had less than 50% of correlations with other items above 0.09. All other items had more than 50% of correlations above 0.09 and most had more than 75% and so were satisfactory. Item-total correlations are shown in table 3. Items 1, 7, 9 and 10 had an item-total correlation of less than 0.20. However, eliminating these items iteratively altered Cronbach's alpha by less than 1.5%. The changes in Cronbach's alpha resulting from elimination of each individual item in turn can be seen in Table 7. For the 20-item questionnaire Cronbach's alpha was 0.69 and this increased only to 0.71 if all four items were excluded.

Principal factor analysis generated only one factor with an eigenvalue above 1 (Factor one - eigenvalue 2.3). Items loaded from 0.026 to 0.46 on this factor. Items 1, 4, 7, 9, 10, 11 and 18 loaded less than 0.3. Elimination of these items iteratively from the factor analysis did not alter the distribution of eigenvalues. There was still only one factor with an eigenvalue greater than one and the distribution of the loadings of the items on this factor was unchanged. Iterative elimination of the items with low loadings on factor analysis from item-total and Cronbach's alpha analyses caused changes of less than 1.5%. When items 1,4,9, 11 and 18 were eliminated there were decreases in alpha, rather than the desired increases.

Table 5: Characteristics of participants (n=467)

Characteristic	Mean (SD) or %
Age	37.8 (5.4)
Height	163.1 (6.4)
Weight	69.6 (13.6)
BMI	26.1 (4.8)
Education level, %	
Grade ten or less	33
Completed grade 12	21
University or other tertiary institution	45
Main financial provider unemployed, %	6
Number of children, median, (range)	2, (0-5)
Family history osteoporosis, %	17
Family history of fracture, %	62
History of fracture, %	29
Currently smoking, %	17
Ever smoked, %	49
Married or de facto, %	72

Table 6: Psychometric characteristics of the OKAT

Characteristic	Result
Flesch Reading Ease	45
D-value	44%
Discriminatory power	0.96
Cronbach's alpha	0.69

Table 7: Psychometric Properties of the OKAT by Item

Item Number	Index of Difficulty	Item Discrimination (%)	Item-total correlation	Cronbach's alpha[a]	Factor Loading
1	0.97	12	0.17	0.69	0.21
2	0.37	63	0.33	0.68	0.42
3	0.43	63	0.34	0.68	0.43
4	0.91	21	0.22	0.69	0.27
5	0.60	67	0.37	0.67	0.46
6	0.20	47	0.33	0.68	0.41
7	0.39	35	0.13	0.70	0.15
8	0.27	45	0.27	0.68	0.32
9	0.26	24	0.14	0.70	0.14
10	0.80	17	0.03	0.70	0.03
11	0.12	28	0.21	0.69	0.27
12	0.66	47	0.26	0.68	0.32
13	0.27	53	0.32	0.68	0.37
14	0.67	61	0.34	0.68	0.41
15	0.52	53	0.28	0.68	0.34
16	0.50	70	0.40	0.67	0.46
17	0.24	48	0.30	0.68	0.36
18	0.06	17	0.22	0.70	0.26
19	0.30	60	0.35	0.68	0.42
20	0.29	50	0.27	0.68	0.33

[a] gives Cronbach's alpha with each item omitted in turn.

4.4 Discussion

The OKAT performed satisfactorily on virtually all components of the analysis. The questionnaire had a lower than preferred Flesch reading ease. This was due to the use of the word osteoporosis in 12 of the 20 items. If this word was removed or substituted for by "thin bones" the Flesch reading ease became highly acceptable. As the word osteoporosis was the most accurate description of the disease about which knowledge was being measured and is widely recognised in the general population [166], its use was retained and the resulting decrease in Flesch reading ease accepted.

The questionnaire had a satisfactory index of difficulty. Item discrimination was satisfactory and Ferguson's sigma was close to the ideal value of 1.0. The three items with a high index of difficulty were retained as it was considered they related to core information about osteoporosis namely, the definition of osteoporosis, female preponderance and the physical activity requirements needed for prevention. Though factor analysis must be interpreted cautiously when analysing dichotomous variables, the fact that the analysis generated only one factor with an eigenvalue above 1 is consistent with osteoporosis knowledge being the main factor being measured by the questionnaire, and this provides some support for the construct validity of the instrument. Certainly, if more than one underlying factor had been found, we would have had cause to question construct validity.

The elimination of the items performing poorly on item-total correlation and principal factor analysis changed Cronbach's alpha by less than 1.5% and had minimal effect on the factor analysis outcome, indicating that the elimination of these items had little

effect on the psychometric qualities of the questionnaire. The 20 item Cronbach's alpha of 0.69 was satisfactory, particularly given that in order to achieve high discriminatory power, a scale must include very easy items as well as very difficult items, which tends to decrease the internal consistency of the scale [188]. The elimination of individual items that performed less well did not alter the overall psychometric properties of the questionnaire and would have reduced the breadth of knowledge covered by the questionnaire ie affected content validity. These items evaluated knowledge of the meaning of osteoporosis, its prevalence, the adverse health outcomes of osteoporosis and of the physical activity requirements for prevention. Previous studies [157, 158] have described the problem of clinically pertinent items not performing ideally under psychometric testing, but still being important for the overall context of the instrument. We dealt with this problem in a similar manner to those studies. If the items contained what we considered to be core knowledge we retained them, but only after (1) examining the psychometric properties with and without the items to ensure that we did not adversely affect the reliability of the questionnaire and (2) describing the reasons for retention and the reasons for considering removing the item.

Baseline levels of osteoporosis knowledge measured using this instrument were low, with the average score of 8.8 being 44% of the possible maximum score. Most other studies of osteoporosis knowledge levels have shown low levels, but these have been in highly selected populations or have not used validated instruments to measure osteoporosis knowledge [130, 149, 151, 154, 155, 160-163]. One study showed knowledge levels of 78% of the maximum score in 16-59 year old Norwegian women but the instrument was not validated [164]. As the average score using our instrument was low, there is scope for the instrument to be sensitive to change, which is a property that will be

valuable if using the questionnaire to assess changes in knowledge with interventions. However, sensitivity to change remains to be tested.

This study has a number of potential limitations. While the sample was randomly selected, selection bias is possible due to the moderate response rate. Indeed the proportion of current smokers in the sample is lower than the Tasmanian prevalence of daily smoking in females aged 25-44 in 1998 of 29% [191] and the proportion of women in married or in a de facto relationship is slightly higher than the Tasmanian proportion of 64%. However, the spread of education levels and the unemployment rate approximates the overall population figures for these variables. The range of demographics covered within the sample means that the validation has occurred over a reasonably heterogeneous group and so the questionnaire appears suitable for use in women aged 25-44 years across a range of demographics. Although the osteoporosis knowledge instrument is based on the OPSMC content and the osteoporosis information leaflet, it covers a broad spectrum of osteoporosis knowledge and may be suitable for use to assess the impact of other osteoporosis educational interventions or to assess osteoporosis knowledge levels in young female Caucasian populations. The OKAT would require validation in other populations and some modifications might be necessary to reflect regional variations in osteoporosis demographics.

In conclusion, the OKAT for measuring osteoporosis knowledge has good psychometric properties in Australian 25-44 year old females. While it should be applicable to other Caucasian populations, this will require confirmation by further research.

Chapter 5: Sociodemographic factors associated with calcium intake in premenopausal women: a cross-sectional study.

5.1 Introduction

Adequate calcium intake is important in the prevention of osteoporosis and may also have a role in prevention of other diseases (see Chapter 1.3). Despite this being widely known, low dietary calcium intakes have been reported frequently [105, 107-111]. The public health importance of this issue is widely recognized and increasing calcium intake has been targeted as part of nutrition policy in Europe, the US and Australia [10, 114, 115].

A high proportion of calcium intake in the diet comes from dairy products [192]. In a 1991 survey of American female meal planners, it has been shown that women are less likely to meet the RDI for calcium if they avoid all types of milk [193]. This finding has not been replicated elsewhere and the magnitude of the association has not been reported. Lower socioeconomic status has been associated with poorer quality diet in general [194-199]. However, few studies have described specific factors associated with low calcium intake. Ethnicity, eating away from home and age less than 25 years have been reported as associated with failing to meet the RDI for calcium in American female meal planners [193, 200]. In the US Department of Agriculture 1985-86 survey of women aged 19-50 years, positive associations were found between higher education, higher income, working part-time and having children in the household and calcium intake [193, 201]. No information is available on possible associations between family or personal history of osteoporosis or fracture, breast-feeding history, smoking history, osteoporosis knowledge or osteoporosis self-efficacy and calcium intake.

The aims of this cross-sectional study were to describe the association between socio-demographic factors and calcium intake in a representative sample of healthy women

aged 25 to 44 years, and to evaluate the association between having low milk intake and meeting the RDI for calcium.

5.2 Methods

The study was carried out in Southern Tasmania, Australia as part of an ongoing study examining the effects of lifestyle factors on bone mineral density in women aged 25-44 years. A full description of the overall study design and methods is given in Chapter 3.

Statistics

The distribution of daily calcium intake was skewed to the right so it was log-transformed. Pearson's correlation coefficient was calculated between variables and log daily calcium intake. Variables which correlated with log daily calcium intake with $p \leq 0.1$ in exploratory analyses were considered for further examination. Univariate analyses were performed using linear regression techniques (continuous variables) and one way analysis of variance (ANOVA) or the Kruskal-Wallis test (categorical variables). Bonferroni, Sidak and Scheffe procedures were performed where there were multiple levels of comparison in one way ANOVA. Results with $p \leq 0.1$ were considered for inclusion in multivariate analysis, as well as including other potential confounders such as age, height (as a surrogate measure of total energy intake) and use of calcium supplements.

Univariate logistic regression was performed to identify potential factors associated with achieving the RDI for calcium. Again factors with $p \leq 0.1$ in univariate analysis were considered for inclusion in multivariate analysis as well as the potential

confounders used above. We calculated the odds of achieving the RDI for calcium with calcium specific self-efficacy and calcium knowledge levels greater than the median value. As there were low numbers of subjects (n=5) in the education to less than grade ten category, education level was initially analysed in three levels (Table 8).

All analyses were performed in Stata version 7 (Stata Corporation, Texas, USA). Statistical significance was set as $p< 0.05$ (two tailed).

5.3 Results

Four hundred and sixty-seven women were recruited into the study (63% response rate). Characteristics of the respondents are given in Table 8. The mean calcium intake was 789 mg (IQR 511-983). The RDI for calcium was met from dietary sources by 40% of women. Regular intake of calcium supplements (more than 4 times per week) was uncommon (2.1%).

One-way analysis of variance for the three levels of education showed that there were statistically significant differences in log daily calcium intake between the three levels. However, there were significant differences in log daily calcium between education up to and including grade ten, and to grade twelve, and between up to grade ten and tertiary education ($p<0.01$), but not between up to grade twelve and tertiary ($p >0.9$) (Figure 1). Education was therefore categorized as a dichotomous variable of either less than or equal to, or greater than grade 10 in further analyses.

Table 9 describes the associations between osteoporosis knowledge and osteoporosis self-efficacy and calcium intake. While total self-efficacy and knowledge both were associated with log daily calcium intake, when the subscales for calcium and non-calcium related items were considered as separate variables, it was the calcium subscales that remained significantly associated with log daily calcium intake in multivariate analysis. Level of education, calcium specific osteoporosis knowledge and calcium specific osteoporosis self-efficacy were positively associated with log daily calcium intake in both univariate and after adjusting for potential confounding in multivariate analysis (Table 10) whereas unemployment of the main financial provider

in the family was associated with lower log daily calcium intake in both analyses. The model accounted for a reasonable proportion of the variation in calcium intake (adjusted R^2 = 13%, p<0.0001). There were no statistically significant associations between log daily calcium intake and past smoking (β = -0.02, 95%CI –0.1, +0.07) or current smoking (β = -0.06, 95%CI -0.2, +0.08), family history of fracture (β = +0.02, 95% CI -.07, +0.1) or personal history of fracture (β = -.07, 95%CI -0.2,+0.04) or having ever breast fed (β = -0.03, 95%CI -0.1,+0.07). Nor were there any associations between age, the hours of employment of the respondents, marital status and log daily calcium intake (data not shown). In current smokers there was no association between log daily calcium intake and the number of cigarettes smoked per day (r = +0.07, p = 0.52). There were weak trends towards lower calcium intakes with higher numbers of children (r = –0.09, p = 0.05) and with higher lifetime levels of smoking (in pack years) (r = -0.09, p = 0.06). These trends did not persist after adjustment for potential confounders.

Table 11 documents the factors associated with reaching the RDI for calcium intake. After adjusting for potential confounding, scoring above the median score for calcium specific osteoporosis knowledge and self-efficacy were both associated with a higher likelihood of achieving the RDI. Interestingly, the magnitude of the effect of the employment status of the main financial provider is increased in multivariate analysis, with the odds ratio decreasing from 0.39 (95% CI 0.15, 0.98) to 0.17 (95% CI 0.034, 0.86)primarily after adjustment for currently smoking.

Table 8: Characteristics of Participants (n=467)

Characteristic	
Dietary calcium intake (mg), mean, median (IQR)	789, 721 (511 – 983)
Proportion using calcium supplements, %	2.1
Age (yrs), mean (sd)	37.8 (5.4)
Height (cm), mean (sd)	163 (6.4)
Weight (kg), mean (sd)	70 (13.6)
BMI (kg/m^2), mean (sd)	26 (4.8)
Number children, median (range)	2 (0-5)
Current smokers, %	17
Main provider employed, %	94
Respondent not in paid employment, %	14
Education level	
Grade 10 or less, %	33
Completed grade 12, %	21
University or other tertiary institution, %	45
Married or defacto, %	72
Prevalent fracture(s), %	29
Family history of fracture present, %	62
Family history of osteoporosis present, %	17
Osteoporosis knowledge (20 items), mean (sd)	8.8 (3.3)
Calcium knowledge (3 items), mean (sd)	1.5 (1.0)
Osteoporosis self-efficacy (Out of 48), mean (sd)	34.4 (7.1)
Calcium self-efficacy (Out of 24), mean (sd)	17.9 (3.9)

Table 9: Associations Between Osteoporosis Knowledge, Self-efficacy and Calcium Intake

	Univariate β	p-value	Multivariate β	p-value
Total Osteoporosis self-efficacy	*0.015*	*<0.001*	*N/A*	
Ca specific self-efficacy	0.027	<0.001	0.022[a]	0.001
Non calcium self-efficacy	0.019	<0.001	0.01[a]	0.11
Total Osteoporosis knowledge	*0.029*	*<0.001*	*N/A*	
Ca specific knowledge	0.13	<0.001	0.11[b]	<0.001
Non calcium knowledge	0.027	0.001	0.010[b]	0.27

[a] Model includes both calcium specific and non-calcium specific osteoporosis self-efficacy

[b] Model includes both calcium specific and non-calcium specific osteoporosis knowledge

Table 10: Factors Associated with Log-Transformed Dietary Calcium Intake

	Univariate β^a (95% CI)		Multivariate β^b (95%CI)	
Education level (≥ grade ten vs < grade10)	**+0.24**	**(+0.15, +0.34)**	**+0.16**	**(+0.06, +0.25)**
Calcium specific osteoporosis knowledge (per unit)	**+0.13**	**(+0.08, +0.17)**	**+0.10**	**(+0.06, +0.15)**
Calcium specific osteoporosis self-efficacy (per unit)	**+0.03**	**(+0.02, +0.04)**	**+0.02**	**(+0.01, +0.03)**
Provider unemployed (yes vs no)	**-0.20**	**(-0.40, -0.009)**	**-0.17**	**(-0.39, -0.01)**
Corticosteroid use (yes vs no)	**-0.20**	**(-0.39, -0.01)**	-0.08	(-0.27, +0.10)
Family history osteoporosis (yes vs no)	+0.11	(-0.02, +0.23)	-0.08	(-0.05, +0.03)
Number of children	-0.04	(-0.07, +0.00)	-0.01	(-0.04, +0.02)

[a] Bold denotes statistical significance.

[b] Adjusted for other items in table, age, height and use of calcium supplements.

Table 11: Factors Associated with Achieving the RDI for Calcium Intake.

	Univariate[a] OR (95% CI)		Multivariate OR[b] (95% CI)	
Education Level (>grade 10 vs up to grade 10)	**1.64**	**(1.09, 2.46)**	1.65	(0.90, 3.01)
Calcium specific knowledge (> median score vs ≤ to median)	**1.63**	**(1.13, 2.37)**	**1.97**	**(1.10, 3.56)**
Calcium specific self-efficacy (> median score vs ≤ to median)	**1.55**	**(1.05, 2.29)**	**1.84**	**(1.00, 3.40)**
Main provider unemployed (yes vs no)	**0.39**	**(0.15, 0.98)**	**0.17**	**(0.034, 0.86)**
Currently smoking (yes vs no)	**0.48**	**(0.27, 0.86)**	**0.46**	**(0.25, 0.86)**
Corticosteroid use (yes vs no)	0.46	(0.19, 1.09)	0.39	(0.078, 1.95)

[a] Bold denotes statistical significance

[b] Adjusted for other items in table as well as age, height and calcium supplement use

A mean of 40% of the participant's calcium intake came from milk. Figure 2 shows the proportion of subjects meeting the RDI in low (<300 ml/day) compared to high (>300 ml/day) milk consumption groups. The proportion of women meeting the RDI for calcium intake was even lower, at 11% if milk consumption was less than 150 ml per day. The odds ratio for achieving the RDI for calcium in women with high compared to low milk intake was 11.2 (95% CI 6.6, 18.7).

Figure 1. Geometric mean calcium (mg) by education level.

Data are presented as mean + SE. While there is a linear trend between daily calcium intake and level of education, there are only significant differences between women educated to a maximum of grade ten, and higher levels, and not between women educated to grade twelve and tertiary levels.

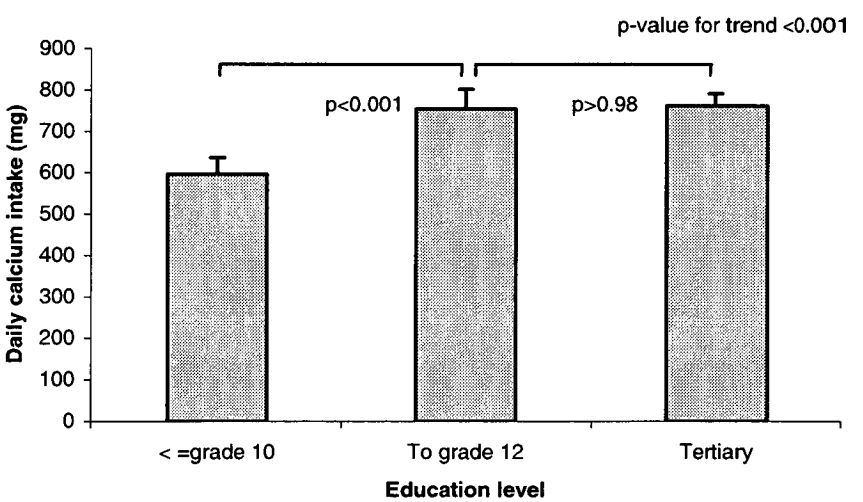
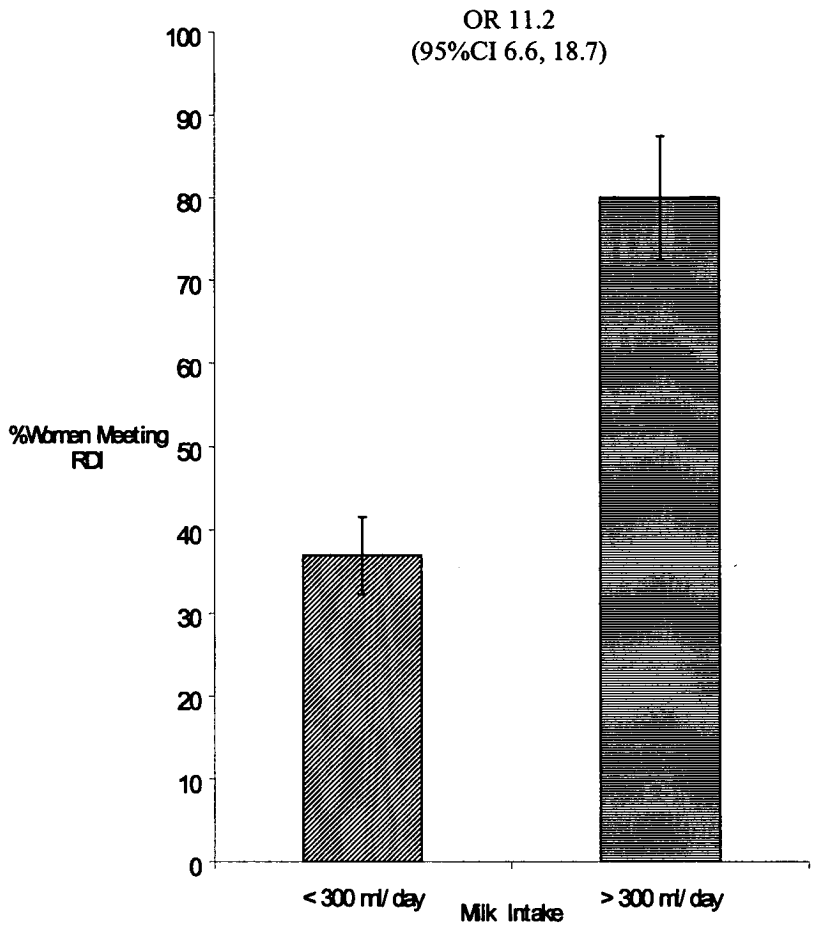


Figure 2: Percentage of women meeting the RDI for calcium by milk intake.

Data are presented as mean and 95% CI.



5.4 Discussion

Consistent with other studies, we report a low calcium intake in premenopausal women, with 60% of women not meeting the RDI for calcium of 800 mg from dietary sources. Furthermore, few women (2.1%) were using calcium supplements. Our study identifies subgroups of premenopausal women who are at greater risk of not meeting their RDI for calcium, and who therefore may be at increased risk of a number of diseases, including osteoporosis, colon cancer and obesity. Importantly, a number of sociodemographic variables were independently able to explain a significant proportion of the variation in calcium intake. Dietary calcium intake was positively associated with levels of calcium-specific osteoporosis knowledge and calcium-specific osteoporosis self-efficacy. In addition, dietary calcium intake was lower when the main financial provider in the household was unemployed and when the highest achieved education level was to grade ten or less.

While it has been commonly reported that lower socioeconomic status is associated with a less healthy diet [194-199], specific associations of sociodemographic variables with calcium intake have been described less frequently. Higher education levels have been associated with higher nutrient density of calcium in the diet of Hong Kong Chinese men and women aged 24-74 years [194]. However, this finding was limited to the ethnic Chinese population, where the difference was mainly noted between primary and higher educational level groups. In our predominantly Caucasian sample, those women who had completed grade ten level (schooling until approximately age 16 years) had a lower mean calcium intake than those who studied at the pre-tertiary and tertiary level (schooling to approximately age 18 years or higher). A positive relationship between

calcium intake and education level was also reported in the 1985-6 Continuing Survey of Food Intakes by Individuals (CSFII) [193] and in the 1990-91 survey of female meal planners above 18 years of age [201]. These surveys did not demonstrate a threshold effect as observed in the current study. The 1990-91 survey was also restricted to female meal planners only, introducing a potential bias in the results. For example, young working women or students might be more likely to be still living with parents and might be under-represented in the sample. Furthermore, neither of these surveys adjusted for potential confounding by a range of factors included in our study. The threshold effect of education, with women educated to grade 10 having lower calcium intakes may indicate that women leaving school at this stage are missing important health education messages with regard to calcium intake. With the known association of low socioeconomic status with poor diet, it may be that other health messages are also being missed in early school leavers. This could be addressed by increasing retention rates of children in the education system. Alternatively, a reassessment of the curriculum could ensure that relevant education relating to calcium intake behaviours takes place before girls leave the school system.

There was also an association between the employment status of the main provider in the family and calcium intake, but no association with the employment status of the respondent. This contrasts with previous findings which described a higher likelihood of meeting the RDI for calcium intake in women who worked part-time [193]. This may reflect the restriction to sampling only female meal planners over the age of 18 years in the previous study, but also may be due to differences in the US and Australian populations, or to changes over time. The observation that the employment status of the main financial provider is positively associated with calcium intake is consistent with

previous findings that increased household income level was also positively associated with higher calcium intake [201]. Current smokers were half as likely to achieve the RDI for calcium compared to non-smokers, independent of other factors. It is of particular concern that smokers have lower calcium intake, given the negative associations between smoking and low bone mineral density in premenopausal women [61] and smoking and decreased intestinal calcium absorption [202]. The negative associations between employment and calcium intake, and smoking and calcium intake identify two target groups for more intensive public health interventions. The lack of an association between events that one might hypothesize could cause a person to actively try to increase their calcium intake, such as breastfeeding or personal or family history of fracture, and calcium intake suggest that these events on their own are unlikely to cause calcium intake behaviour change. Women who have experienced these events need at least the same degree of public health intervention as women without such histories.

The total scores for both osteoporosis knowledge and self-efficacy were positively associated with calcium intake. Further analysis revealed that this was largely due to the calcium specific items in both instruments. Bandura [168] describes four main influences on self-efficacy, being mastery experiences, vicarious experiences (or modeling), social persuasion and somatic and emotional states. Possible explanations for the positive association between calcium intake and calcium self-efficacy are that those women who were already successful in having higher levels of calcium in their diet (a mastery experience), or that women who came from family backgrounds where high calcium intake had been modeled, were more confident that they could increase or maintain this. Achieving higher levels of calcium-specific self-efficacy might also be possible within the education system by modeling such behaviours in schools. While

numerous different interventions have been used to increase self-efficacy in a number of health-related areas, of particular interest is the use of an exercise prescription instrument by primary care physicians, which resulted in increases in exercise self-efficacy [203]. This raises the possibility of the development of a calcium intake prescription along the same lines. However, further social and behavioural research is needed to determine the reasons why some women have higher levels of calcium-specific self-efficacy and to examine how calcium-related self-efficacy might best be improved. Levels of calcium specific knowledge were low, with the mean score similar to that expected from chance alone. The positive association between calcium-specific osteoporosis knowledge and calcium intake suggests that if a person has more knowledge about calcium, they would be better equipped to increase their calcium intake. This has been demonstrated in the context of exercise and calcium intake behaviour for osteoporosis prevention [156]. It remains to be seen if changing levels of knowledge and/or self-efficacy result in improved calcium intake behaviour in prospective trials.

Previous studies have reported that a significant proportion of calcium intake is from milk sources [105, 192]. In our study, 40% of the calcium intake came from milk. Only 37% of women who drank less than 300 ml of any type of milk per day met their RDI for calcium, compared to 80% of women who drank more than 300 ml of milk per day (Figure 2). The proportion of women meeting the RDI dropped to just 11% if milk intake was less than 150 ml per day. The odds of meeting the RDI for calcium were over 11 times higher in women who drank more than 300 ml of milk per day compared to those who did not. While the odds ratio overestimates relative risk, the impact of low milk consumption clearly is nonetheless substantial. Similar results have been reported

in the US in women who avoided all types of milk [193], but our results show that having even a moderately low milk intake is associated with a markedly increased risk of not meeting the RDI. There may be some difficulty in encouraging women to alter their diet in this regard. In one study it has been reported that 77% of women who consumed fewer than two servings of milk products a day had no intention of increasing their consumption [204]. Health promotion programs need to specifically address how to approach the sub-group of women who have low milk intake, and aim to either increase consumption of milk or encourage calcium intake from other sources.

This study has a number of potential limitations. While the sample was randomly selected, selection bias is possible due to the moderate response rate. The proportion of current smokers in the sample is lower than the Tasmanian prevalence of daily smoking in females aged 25-44 years in 1998 of 29% [191] and the proportion of women in married or in a de facto relationship is slightly higher than the Tasmanian proportion of 64%. However, the wide spread of education levels and the unemployment rate approximates the overall population figures for these socioeconomic factors and the results persisted after adjustment for these variables. Furthermore, calcium intake in this study is only slightly higher than that reported in a Southern Tasmanian sample of women who were selected using criteria that resulted in a cohort with high levels of smoking [61]suggesting that while there is a potential for selection bias towards a healthy cohort, the effects of this are minor and the results of this study may be generalized to healthy Caucasian women in the 25 to 44 year age range. A short food frequency questionnaire was chosen to measure calcium intake due to its ease of administration to large numbers of people. It is recognized that the questionnaire will underestimate calcium intake [179]. The effect of this measurement error is that the proportion of women meeting the RDI

for calcium may be underestimated. However, the resulting misclassification is likely to dilute any associations, suggesting that the real associations may be greater than those reported. The FFQ does not measure total dietary energy intake so we were unable to calculate nutrient densities. However, adjusting for height and age as crude indicators of energy intake did not materially affect the results of the study. It is also noted that while the multivariate model accounted for a reasonable proportion of the variation in calcium intake, a substantial amount remains unexplained by the factors measured in this study. Further research is required to identify other potential factors influencing calcium intake.

In conclusion, women who have lower levels of education, who are in households where the main financial provider is unemployed, who are smokers, and those with low levels of calcium-specific self-efficacy and knowledge, are at risk of not achieving adequate calcium intake. This information will inform public health strategies aimed at improving the calcium intake of women in this age group.

Chapter 6: The Effects of Bone Density Feedback and Group Education on Osteoporosis Knowledge and Osteoporosis Self-efficacy in Premenopausal Women.

6.1 Introduction

Osteoporosis self-efficacy and osteoporosis knowledge have been demonstrated to be important determinants of exercise and calcium intake behaviours relevant to the prevention of osteoporosis [153, 156]. Osteoporosis knowledge levels have been found to be low in a variety of populations [130, 151, 161-164, 166, 167, 175]. Despite this, there is limited information about how best to improve osteoporosis knowledge and osteoporosis self-efficacy at a population level.

Three randomised controlled trials (RCT) of similar single-session osteoporosis education programs [126, 162, 175] have all demonstrated increases in short-term osteoporosis knowledge but only one demonstrated an increase in osteoporosis self-efficacy [162]. Another study using written information for education [128] reported a short-term increase in knowledge levels that did not persist at 12 months.

One uncontrolled study using an information booklet with patients self-selecting for bone mineral density measurement with discussion of results by a nurse, and/or a one-hour osteoporosis education workshop [130], suggested an information leaflet was as effective at increasing knowledge as the workshop, and that bone density screening also increased knowledge levels. Other studies [131, 132] suggest that feedback of BMD to premenopausal women may also be effective at changing osteoporosis prevention behaviours, but there is no published data demonstrating the effect of BMD feedback on levels of osteoporosis knowledge or osteoporosis self-efficacy levels. Furthermore, it is not known whether BMD feedback and educational interventions produce independent effects on osteoporosis knowledge and osteoporosis self-efficacy.

The aim of this study therefore, was to compare the effects of BMD feedback and two educational interventions, group-based behavioural education and an osteoporosis information leaflet, on short and longer-term changes in osteoporosis knowledge and osteoporosis self-efficacy in women aged 25-44 years.

6.2 Methods

See Chapter 3 for a description of the overall study methods and Chapter 4 for a description of the psychometric properties of the OKAT.

Statistics:

Differences between knowledge and self-efficacy scores over time were assessed using paired t-tests or the Wilcoxon signed-rank test depending on the distribution of the data. Univariate and multivariate linear regression was used to examine the predictors of changes in both scores, examining the effects of the educational intervention, T-score group and sociodemographic variables (age, employment status of main financial provider in the household, employment status of subject, education level of subject, marital status, number of children, current smoking, history of having ever smoked, family or personal history of fracture, family history of osteoporosis, history of corticosteroid use, eating disorder or asthma). The analysis was performed by intention to treat, and per protocol defined in two ways: firstly, by whether subjects attended at least one of four educational session of the OPSMC, and secondly, by whether they attended all four OPSMC sessions.

Oneway ANOVA, the Kruskal-Wallis test or chi-squared testing was used as appropriate to examine differences in characteristics between subjects completing and those withdrawing from the study and between intervention groups.

All analyses were performed in Stata version 7 (Stata Corporation, Texas, USA). Statistical significance was set as $p< 0.05$ (two tailed).

6.3 Results

A total of 470 women were recruited with a response rate of 64%. The characteristics of subjects completing the study (n=415) and those who withdrew (n=55) are given in Table 12. There were no statistically significant differences between subjects completing and those withdrawing from the study. However, withdrawals tended to have lower levels of education and a greater proportion came from a household in which the main financial provider was unemployed.

Baseline characteristics of the different intervention groups (Group 1 = Randomised to leaflet, T-score 0 or above so received feedback of not being at increased risk of fracture in later life; Group 2 = Randomised to OPSMC, T-score 0 or above so received feedback of not being at increased risk of fracture in later life; Group 3 = Randomised to leaflet, T-score < 0 so received feedback of being at higher risk of fracture in later life; Group 4 Randomised to OPSMC, T-score < 0 so received feedback of being at higher risk of fracture in later life) are given in Table 13. Of the 470 subjects, 236 had a mean T-score of greater than or equal to 0. There were 248 subjects who received the information leaflet and 219 received the OPSMC. Despite randomisation, subjects in

the groups receiving the OPSMC had higher baseline levels of knowledge than groups receiving the information leaflet ($p<0.05$). There were no statistically significant differences in stage of change across intervention groups.

The average baseline osteoporosis knowledge score was 8.8/20 (s.d 3.3). All intervention groups showed a statistically significant increase in knowledge score at 6 weeks, ranging from 2.9 to 4.9 units ($p <0.0001$ in all groups). The greatest increase in knowledge occurred in group 4 (low mean T-score and OPSMC). At two years knowledge scores remained higher than at baseline in all intervention groups ($p<0.0001$), despite a drop in knowledge scores from the 6-week scores of between 0.8 and 1.8 units (p range 0.0002 – 0.05).

Table 12: Comparison of characteristics of participants and withdrawing subjects.

Characteristic[a]	Completed study (n=415)	Withdrawals (n=55)
Age (yrs), mean (SD)	38.1 (5.2)	35.4 (5.8)
Mean T-score<0, %	51	40
Received OPSMC, %	47	44
Height (cm), mean (SD)	163.0 (6.4)	164.0 (6.3)
Weight (kg), mean (SD)	69.6 (13.5)	68.9 (14.0)
BMI (kg/m^2), mean (SD)	26.2(4.8)	25.7 (5.2)
Education level, %		
<Grade 10	32	43
Grade 11-12	21	20
>Grade 12	46	38
Provider unemployed,%	6	9
Employment status, %		
0 hrs/week	14	15
<20 hrs/week	24	21
>20 hrs/week	63	66
Number of children median, mean (sd)	2,1.7 (1.2)	2, 1.4(1.5)
Family history osteoporosis, %	17	23
Family history of fracture, %	39	31
Prevalent fracture(s), %	28	31
Currently smoking, %	32	26
Ever smoked, %	53	42
Married or de facto, %	74	69

[a] $p<0.05$ for all comparisons between completing and withdrawing subjects

Table 13: Comparison of characteristics of participants in each intervention category.

	Group 1	Group 2	Group 3	Group 4
Characteristic	T-score ≥ 0 and leaflet (n=128)	T-score ≥ 0 and OPSMC (n=108)	T-score<0 and leaflet (n=120)	T-score<0 and OPSMC (n=111)
Age (yrs)), mean (SD)	37.9 (5.3)	37.4 (5.8)	38.4 (5.0)	37.4 (5.3)
Baseline knowledge (out of 20, mean (SD))	8.4 (2.9)	9.4 (3.5)	8.4 (3.4)	9.1 (3.4)
Baseline self-efficacy (out of 48, mean (SD))	34.4 (7.4)	35.0 (7.1)	34.1 (7.3)	33.7 (6.5)
Education level, %				
<Grade 10	28	41	38	29
Grade 11-12	27	14	22	21
>Grade 12	46	45	41	50
Provider unemployed,%	5	6	10	3
Employment status, %				
0 hrs/week	16	11	14	13
<20 hrs/week	21	24	26	22
>20 hrs/week	63	65	60	64
Number of children, median	2	2	2	2
Family history osteoporosis, %	16	12	23	17
Family history of fracture, %	62	60	61	64
Prevalent fracture(s), %	27	24	33	30
Currently smoking, %	20	16	18	13
Ever smoked, %	51	44	57	41
Married or de facto, %	68	80	71	75
Calcium Intake (mg/day)	805 (429)	795 (406)	753 (368)	803 (389)
Calcium Supplement Use, %	1	0	3	4
Median Strenuous Activity Level	3	3	3	3

Figure 3 (a) and (b) shows the changes in osteoporosis knowledge over the study period by T-score group and by educational intervention. In univariate analysis, changes in osteoporosis knowledge were associated with both receiving the OPSMC and with low T-score group (Table 14). Of the sociodemographic variables examined, only history of having ever smoked, was significantly associated with changes in knowledge score (β = +0.85, 95%CI +0.24, +1.46). There was no association between stage of change and change in knowledge score. After adjusting for potential confounders, the OPSMC was associated with an increase in knowledge score in both the short and long term. However, the increase in knowledge seen at 6 weeks did not persist at the same magnitude at 2 years. This contrasts with the effect of feedback of low T-score, which showed a trend towards increase in knowledge in the short-term, which persisted and became statistically significant at 2 years. The effects of the OPSMC and of T-score group were similar whether the analysis was performed by intention to treat or by per protocol analysis (Table 14).

Figure 3: Change in osteoporosis knowledge score by (a) T-score group (b) educational intervention. Error bars show 95% CI.

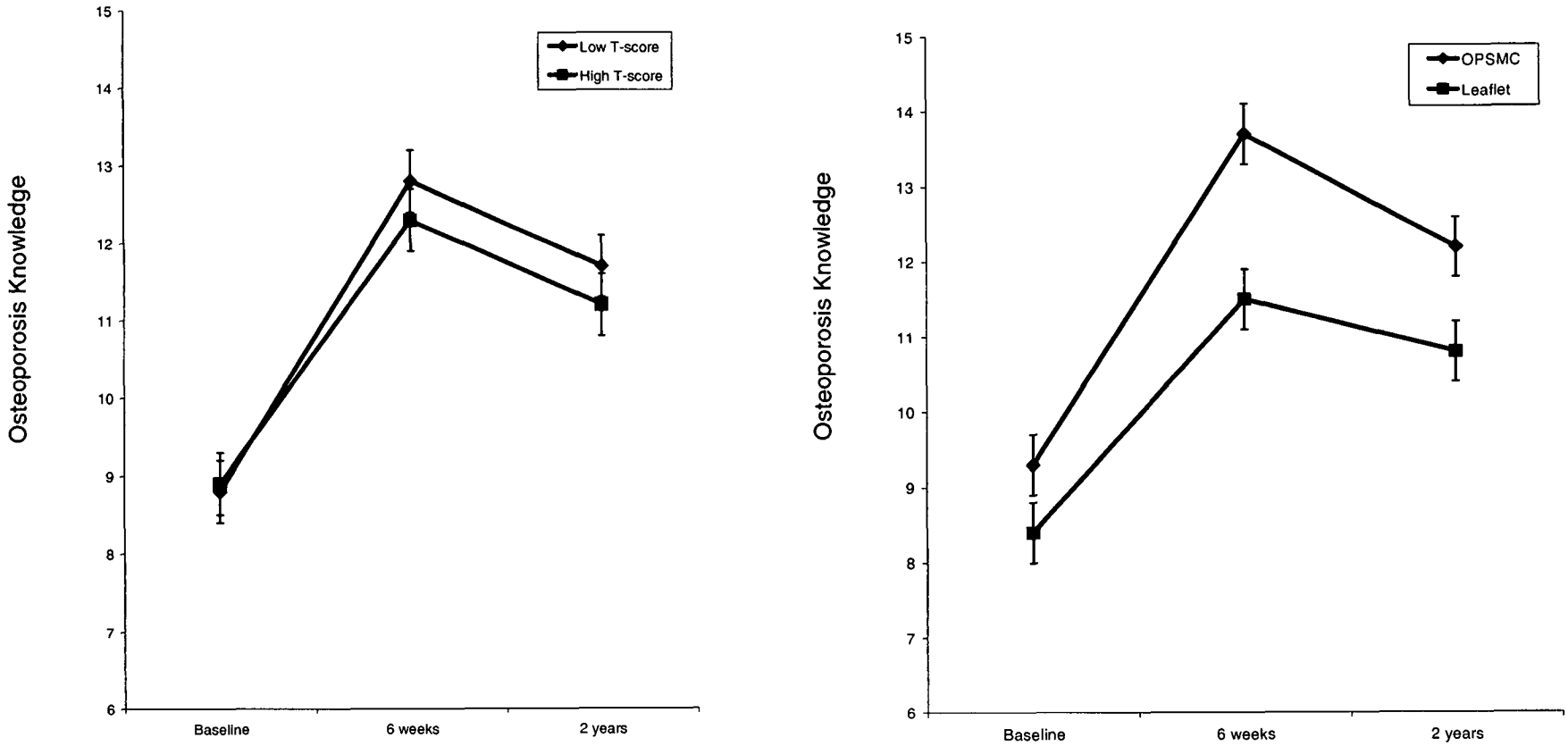


Table 14: Effects of Interventions on Changes in Knowledge

	Univariate[a,c] (95% CI)	Multivariate[b,c] (95% CI)	Multivariate[b,d] (95% CI)	Multivariate[b,e] (95% CI)
Change in knowledge, baseline to 6 weeks				
OPSMC	**+1.35 (+0.75, +1.95)**	**+1.33 (+0.72, +1.94)**	**+1.80 (+1.18, +2.42)**	**+1.46 (+0.70, +2.22)**
T-score group (>= 0 or < 0)	**+0.64 (+0.037,+1.25)**	+0.57 (-0.036, +1.17)[f]	+0.51 (-0.08, +1.10)[f]	+0.52 (-0.09, +1.12[f]
Change in knowledge, baseline to 2 years				
OPSMC	+0.56 (-0.028, +1.18)[f]	**+0.64 (+0.0034, +1.25)**	**+1.25 (+0.63, +1.86)**	**+0.80 (+0.07, +1.53)**
T-score group (>= 0 or < 0)	**+0.69 (+0.087,+1.29)**	**+0.66 (+0.064, +1.26)**	**+0.63 (+0.04, +1.23)**	**+0.66 (+0.06, +1.26)**

[a] bold denotes statistical significance.

[b] adjusted for other items in table, education level, history of ever smoking and age.

[c] intention to treat analysis

[d] per protocol analysis defined as attending at least one educational session

[e] per protocol analysis defined as attending all educational sessions

[f] $p<0.1$

Overall, there was a decrease in self-efficacy from 34.3/48 to 33/48 in the first year ($p<0.001$ for difference) which persisted at 2 years ($p<0.001$). Figure 4 shows that osteoporosis self-efficacy fell over the course of the study in all 4 groups. By two years, the decrease in groups 1 (T-score ≥ 0, leaflet), 2 (T-score ≥ 0, OPSMC) and 4 (T-score < 0, OPSMC) were statistically significant (all $p<0.05$) with a trend in group 3 (T-score < 0, leaflet) ($p=0.08$). In univariate analysis, both short-term and long-term changes in osteoporosis self-efficacy were negatively associated with the number of children and hours of employment but not with other sociodemographic factors nor with stage of change. The associations remained after adjusting for potential confounders (Table 15). There were no associations between low T-score or receiving the OPSMC and changes in osteoporosis self-efficacy. The adjusted associations were similar whether intention to treat or per protocol analysis was performed (data not shown).

Figure 4: Changes in self-efficacy by intervention group. Points show mean osteoporosis self-efficacy in each group at each measurement time.

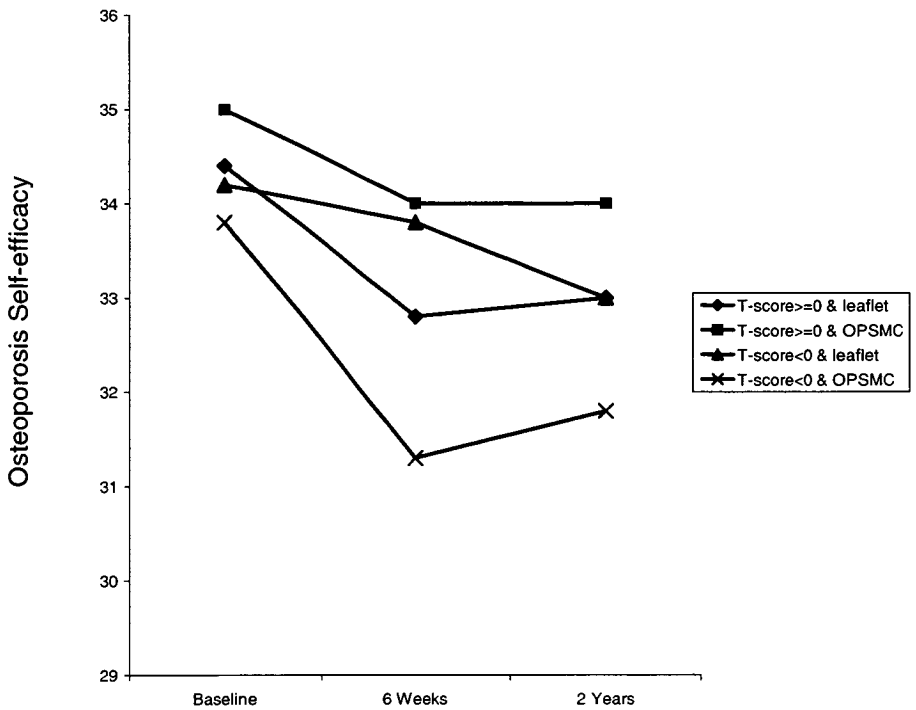


Table 15: Factors affecting change in osteoporosis self-efficacy

Self-efficacy Change 0 to 1 year	Univariate[a]	(95% CI)	Multivariate[b]	(95% CI)
Smoker	+1.4	(-0.3, +3.1)	+1.3	(-0.4, +3.1)
No. of children	**-0.7**	**(-1.2, -0.2)**	**-0.9**	**(-1.4, -0.3)**
Employment level				
0 hours per week	0.0		0.0	
<20 hours per week	-1.5	(-3.5, +0.6)	-1.6	(-3.7, +0.5)
>20 hours per week	**-1.9**	**(-3.7, -0.02)**	**-2.7**	**(-4.6, -0.8)**
OPSMC	-0.6	(-1.9, +0.6)	-0.6	(-1.8, +0.6)
T-score group (≥ 0 or < 0)	-0.02	(-1.2, +1.2)	-0.002	(-1.2-1.2)
Self-efficacy Change 0 to 2 year				
Smoker	-1.0	(-2.8, +0.8)	-1.1	(-2.9, +0.7)
Number of children	-0.5	(-1.0, +0.01)[c]	**-0.7**	**(-1.3, -0.1)**
Employment level				
0 hours per week	0.0		0.0	
<20 hours per week	-1.4	(-3.5, +0.8)	-1.5	(-3.7,+0.6)
>20 hours per week	-1.5	(-3.5, +0.4)	**-2.1**	**(-4.0, -0.1)**
OPSMC	-0.3	(-1.6, +1.0)	-0.1	(-1.4, +1.2)
T-score group (≥ 0 or < 0)	-0.6	(-1.8, +0.7)	-0.6	(-1.9, +0.7)

[a] bold denotes statistical significance.

[b] adjusted for other items in table, education level and age

[c] p=0.05

6.4 Discussion

This study demonstrates that osteoporosis knowledge, but not self-efficacy, can be increased by bone density feedback and a group education intervention (OPSMC), with the effects being additive and independent. While all intervention groups had both short and long term increases in osteoporosis knowledge, the increases were greatest in women receiving feedback of low T-score and in women receiving the OPSMC. The initial marked increase in knowledge from the OPSMC had reduced somewhat by 2 years but remained statistically significant compared with baseline. In contrast, feedback of low BMD was associated with a smaller, non-significant short-term increase in osteoporosis knowledge, which increased slightly in magnitude to become significant at two years. These different patterns of knowledge change may represent different mechanisms of gain in knowledge. For example, women with low T-scores may have accessed information over time from different sources such as health professionals, family members and friends.

Most previous studies have examined only the short-term impact of osteoporosis education interventions in small highly selected groups of women, reducing the generalisability of the studies' results. Two studies [128, 167] have used random sampling to recruit subjects. Blalock found that provision written information caused increases in osteoporosis knowledge, but the response rate was low, again reducing generalisability. Waller describes the impact of a community intervention in Sweden on osteoporosis knowledge. While individuals were randomly selected to take part in the study, subjects were invited, rather than randomly assigned to receive written information and have bone mineral density testing, introducing potential for selection bias. While these

studies showed increases in osteoporosis knowledge with provision of written information, ours is the first population-based study to test the effectiveness of a group education program and BMD feedback in changing levels of osteoporosis knowledge in a randomised controlled trial. Our results indicate an increase in short-term osteoporosis knowledge of about 14% from baseline attributable to the OPSMC, but no significant self-efficacy change. Because of differences in interventions, sampling methods and statistical methods, it is difficult to compare our outcomes directly with those in other studies. To demonstrate this, two studies using the same intervention gave quite different magnitudes of results in different settings. Sedlak's study of the effects of a single education session in a convenience sample of young college women demonstrated an increase of 34% in knowledge in the experimental group compared to 9% in controls, that is a net increase of 23% and no increase in osteoporosis self-efficacy [175]. In contrast, Piaseu tested the same intervention in Thai nursing students and found an increase of 70% in knowledge and 11% increase in self-efficacy [162]. These results were not adjusted for potential confounders and were obtained in highly selected groups. While our results showed smaller change, this was after adjusting for potential confounders and was in a more heterogeneous, less educated and potentially less-motivated population-based sample.

While there was no association between being a current smoker and osteoporosis knowledge changes, having ever been a regular smoker was positively associated with long-term gains in osteoporosis knowledge. This effect was independent of indicators of socioeconomic status. It may be that people who have ever smoked are in fact more receptive to education about osteoporosis. In our study, for example, there were 220 ever smokers and 133 current smokers. Twenty-one percent of the study population and

therefore 40% of the ever smokers were in fact ex-smokers, who had already made a positive health-related lifestyle change. More research is needed to explore potential explanations for the greater increase in knowledge seen in ever-smokers. No other sociodemographic factors were associated with 1-year or 2-year changes in knowledge, nor were personal or family history of any illnesses which might affect the predisposition to learn about osteoporosis.

The finding that osteoporosis self-efficacy, that is, the subjects' confidence in their ability to change calcium intake and physical activity levels, decreased over the duration of the study is unexpected. Changes in osteoporosis self-efficacy were independent of T-score status, or type of education intervention, but both 1-year and 2-year changes in osteoporosis self-efficacy were negatively associated with both number of children and hours of employment. The OPSMC was modeled upon a chronic disease self-management course for arthritis, which has been shown to be modestly effective in symptomatic populations at reducing health care utilisation and improving health status [173, 174]. However, this sample of women was asymptomatic, and thus may have differed from a symptomatic population in many factors, such as in their levels of motivation. This may in part explain why the OPSMC did not improve self-efficacy levels. Bandura [168] describes four main influences on self-efficacy, being mastery experiences, vicarious experiences (or modeling), social persuasion and somatic and emotional states. However, there is evidence that there are other internal personal factors and external environmental factors which are determinants of self-efficacy and that the degree of change in self-efficacy is partly a function of the variability and the controllability of its determinants [205]. In terms of sociodemographic variables, higher levels of exercise self-efficacy have been associated with higher levels of income [171].

Higher levels of general self-efficacy have been associated with being employed [206] and being divorced rather than married [206] and higher levels of education [206, 207]. It is clear from our study that the determinants of change in osteoporosis self-efficacy are more related to the sociodemographic variables of employment status and number of children, than the interventions performed. As discussed by Horan [169], Bandura relates self-efficacy to behaviour in three ways: the conviction that one has the ability to (a) initiate the activity, (b) maintain the activity and (c) persist in performing the activity in the face of obstacles. It is likely that factors associated with working more than 20 hours per week and with having higher numbers of children, such as time pressure, would impact on self-perceived ability to initiate, maintain and persist in changes in osteoporosis preventive behaviour. Self-efficacy is potentially one of the most important and modifiable predictors of physical activity [171] and has been reported as the strongest predictor of a health-promoting lifestyle [172], so the finding that women had a decrease in osteoporosis self-efficacy over the study period is of concern. The degree of concern depends on how much changes in self-efficacy affect changes in osteoporosis preventive behaviours, an issue which needs further research. The study highlights a subgroup of women, working mothers, who may need different interventions to counteract the effects of these sociodemographic changes on osteoporosis self-efficacy.

This study has a number of potential limitations. While the sample was randomly selected, selection bias is possible due to the moderate response rate. The proportion of current smokers in the sample is lower than the Tasmanian prevalence of daily smoking in females aged 25-44 years in 1998 of 29% [191] and the proportion of women in married or in a de facto relationship is slightly higher than the Tasmanian proportion of 64%. Furthermore, the wide spread of education levels and the unemployment rate

approximates the overall population figures for these socioeconomic factors. Adjustment was performed for these and other potential confounders. As discussed in Chapter 5, the calcium intake in this cohort is only slightly higher than that reported in a Southern Tasmanian sample of women who were selected using criteria that resulted in a cohort with high levels of smoking [61]. This suggests that while there is a potential for selection bias towards a healthy cohort, that the effects of this are minor and the results of this study are likely to be generalisable to healthy Caucasian women in the 25 to 44 year age range. The T-score cut off for increased fracture risk was based on data from an older patient population, as discussed in the methods. While direct data from a younger female population would clearly be desirable, in its absence we would contend that we have made the best assessment possible from data currently available in order to produce meaningful feedback to participants. Because the OPSMC was modeled upon a chronic disease self-management course for arthritis effective in symptomatic populations [173, 174], which are likely to be different from the healthy, asymptomatic participants in the current study, further research is required to address the OPSMC's role in the management of other populations of women such as women with existing osteoporosis and/or fracture.

In conclusion, both the OPSMC and bone density feedback increased osteoporosis knowledge but not self-efficacy over two years. Women with children who are also in the workforce decreased osteoporosis self-efficacy over two years, suggesting that this group should be a specific target for interventional strategies. Further research is needed to determine whether changes in osteoporosis knowledge and/or self-efficacy leads to changes in BMD in the medium term and fracture risk in the very long term.

Chapter 7: The Effect on Behaviour and BMD of Individualised Bone Mineral Density Feedback and Educational Interventions in Premenopausal Women: a Randomised Controlled Trial.

7.1 Introduction

Low bone mineral density (BMD) is a major risk factor for osteoporotic fracture [39]. BMD in later life is a function of peak bone mass and the rate of subsequent bone loss [30]. Premenopausal women have significant age-related BMD loss [19-21] and premenopausal bone mass contributes to fracture risk in later life [31]. Modifiable risk factors for low BMD include low calcium intake, smoking and low levels of physical activity [125]. Limited information is available currently on how to influence these risk factors in premenopausal women. Studies have suggested that BMD screening with feedback of results combined with an information leaflet increases self-reported osteoporosis preventive behaviour change at twelve months [130-132]. In particular, greater changes were reported in women with low BMD. However, there have been no longer-term follow-up studies or studies of the effect, if any, of these behaviour changes on BMD. Similarly, studies of educational interventions in pre-menopausal women that have not included a bone density feedback component [126-128, 155] have been short-term and have not studied effects of behaviour change on BMD.

The aim of this study was to determine the effects of individualised bone mineral density (BMD) feedback and two different educational interventions on osteoporosis preventive behaviour and 2-year change in BMD in pre-menopausal women. Specifically, we aimed to test the following hypotheses:

1. Women are more likely to change calcium intake and physical activity if their BMD is low.

2. Group education (in the form of the Osteoporosis Prevention and Self Management course) will be more efficacious at changing these lifestyle behaviours than an information leaflet alone.
3. Bone density feedback and educational intervention have independent effects on behaviour and BMD change.
4. Women who improve their physical activity or dietary calcium intake will have a change in bone mass over 2 years that is 0.34-0.54% per annum better (depending on site and lifestyle factor) than those who do not alter their behaviour.

7.2 Methods

See Chapter 3.

Statistical Analysis

All statistical analyses were based on the à priori hypotheses above. Statistical power calculations are described in Chapter 3. Paired t-tests were performed to compare baseline and 2 year femoral neck and lumbar spine BMD for the whole study sample, and one-way ANOVA to compare BMD within the four intervention groups. Simple linear regression and one-way ANOVA were used for continuous and categorical measures respectively to examine the relationships between BMD change and intervention groupings, and changes in osteoporosis preventive behaviours. Multiple regression modeling, including potential confounders, was then used to examine the relationships between T-score group and educational intervention and BMD change as well as changes in behaviour and BMD change, at both the femoral neck and lumbar

spine. A number of behaviours were measured in different ways, for example changes in physical activity, smoking, calcium intake and calcium supplement use were measured by detailed questionnaires, as well as by simple self-report (change in behaviour - yes/no). In our modeling, we assessed associations between changes in BMD and each method of measuring a behaviour separately. In multivariate analysis, for behaviours measured in more than one way, we reported the effects using the using most objective measure e.g. FFQ assessment of calcium supplement use and dietary calcium intake rather than simple self-report of changes in calcium supplement use and dietary calcium. For simple self-reported physical activity change and smoking change, which were measured at both 1 and 2 years, we reported on effects of persistent improvement i.e. improved behaviour reported at both 1 and 2 years.

The analysis was performed 3 ways:

(1) by available data analysis, which included all subjects who reached 2 years of follow-up;

(2) by intention to treat, in which all randomised individuals were included in the analysis. We imputed missing data at 2 years using the method of last observation carried forward [208] for measured variables, and imputed no change for self-reported behavioural change variables; and

(3) by per protocol analysis defined in two ways: firstly, by whether subjects attended at least one of four educational session of the OPSMC, and secondly, by whether they attended all four OPSMC sessions.

A sensitivity analysis was also performed omitting subjects with a baseline T-score < -2.5, which may lead to pharmacological treatment for osteoporosis in our location. No adjustment was performed for multiple comparisons.

All analyses were performed in Stata version 7 (Stata Corporation, Texas, USA). Statistical significance was set as $p< 0.05$ (two-tailed).

7.3 Results

A total of 470 women (response rate of 64%) were recruited. Of these, 415 (88%) reached final follow-up. Figure 5 shows the flow of subjects through the trial. There were no statistically significant differences in baseline demographics or in proportions of participants receiving the OPSMC and low T-score feedback between those completing the study and those withdrawing.

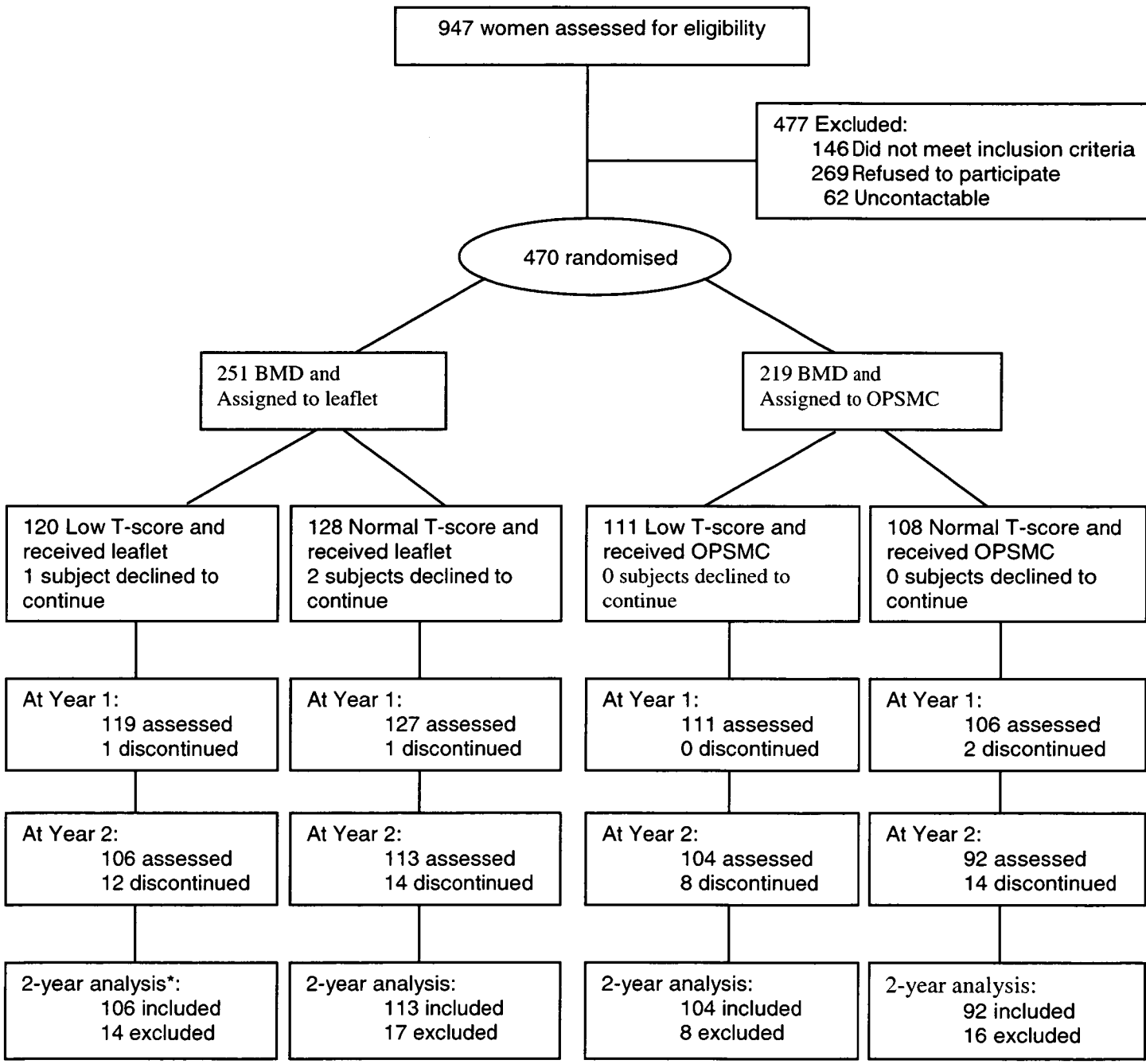
Table 16 shows the baseline characteristics of women in each intervention group. As expected, women in the low T-score categories, were shorter and lighter than those in the high T-score category. There was a trend ($p=0.05$) for a greater proportion of women in the low T-score groups to be taking calcium supplements, but the proportion in both groups was small. The groups were otherwise similar. Only three subjects had a femoral neck or lumbar spine T-score of less than –2.5.

Across the whole study sample, from baseline to 2 years there was a 1.1% p.a. (95%CI +0.9, +1.4) increase in femoral neck BMD from baseline to 2 years and no change in lumbar spine BMD (+0.09 %p.a., 95%CI -0.06, +0.20).

Table 17 compares BMD changes between low and high T-score groups and between the leaflet and OPSMC educational intervention groups. Subjects in the low T-score

group had a greater percentage rate of change in femoral neck BMD as well as higher absolute change (Figure 6). By comparison, there was no difference in the rate of change in femoral neck BMD between the leaflet and OPSMC groups. There were no differences in rates of lumbar spine BMD change between either T-score or education groups.

Figure 5: Flow of subjects through the trial



* Subjects were only excluded from the 2-year analysis if they had discontinued the study before 2 years of follow-up.

Table 16: Comparison of baseline characteristics of each intervention group.

	T-score ≥ 0 and leaflet (n=128)[a]	T-score ≥ 0 and OPSMC (n=108)	T-score<0 and leaflet (n=119)	T-score<0 and OPSMC (n=112)
Age (years)	37.9 (5.3)	37.4 (5.8)	38.4 (5.0)	37.4 (5.3)
Height (cm)	164.2 (6.4)	164.2 (5.6)	162.7 (6.5)	161.5 (6.5)
Weight (kg)	73.9 (15.2)	75.3 (13.6)	65.4 (10.0)	63.5 (10.8)
BMI (kg/m^2)	27.5 (5.7)	27.9 (4.4)	24.8 (4.1)	24.4 (4.0)
Femoral Neck BMD (g/cm^2)	1.01 (0.09)	1.03 (0.11)	0.83 (0.08)	0.84 (0.12)
Lumbar Spine BMD (g/cm^2)	1.16 (0.09)	1.18 (0.10)	0.99 (0.07)	0.99 (0.08)
Calcium Intake (mg/day)	805 (429)	795 (406)	753 (368)	803 (389)
Calcium Supplement Use, %	1	0	3	4
Work Capacity (W)[b]	2.3 (0.7)	2.3 (0.7)	2.3 (0.7)	2.3 (0.6)
Average Leg Strength (kg)[b]	1.3 (0.4)	1.3 (0.4)	1.4 (0.4)	1.4 (0.4)
Median Strenuous Activity Level	3	3	3	3
Currently smoking, %	20	16	18	13

[a] mean (SD) unless otherwise stated [b] per kg body weight

Table 17: Effect of bone density feedback and group education on BMD change.

	Univariate β (95% CI)		Multivariate β[a,b] (95% CI)		Multivariate β[a,c] (95% CI)		Multivariate β[a,d] (95% CI)	
Femoral Neck BMD change (% p.a.)								
T-score (<0 vs >0)	**+0.93**	**(+0.46,+1.4)**	**+0.86**	**(+0.39,+1.34)**	**+0.85**	**(+0.38,+1.30)**	**+0.86**	**(+0.39,+1.34)**
OPSMC v leaflet	+0.22	(-0.26,+0.70)	+0.14	(-0.32,+0.62)	+0.38	(-0.20,+0.96)	+0.19	(-0.29,+0.68)
Lumbar Spine BMD change (% p.a.)								
T-score (<0 vs >0)	+0.02	(-0.29,+0.32)	-0.01	(-0.32,+0.30)	-0.02	(-0.32,+0.30)	-0.01	(-0.32,+0.30)
OPSMC v leaflet	+0.10	(-0.21,+0.40)	+0.09	(-0.21,+0.40)	+0.21	(-0.16,+0.59)	+0.02	(-0.30,+0.34)

[a]adjusted for other items in column, age, and difference in weight and height between baseline and 2 years.

[b] available data analysis

[c]per protocol analysis defined as subjects attending all OPSMC sessions

[d] per protocol analysis defined as subjects attending at least one OPSMC session

Figure 6: Change in BMD by T-score group and educational intervention over 2 years. P-values are comparisons between T-score and between educational groups. Data is presented as mean and upper 95th CI.

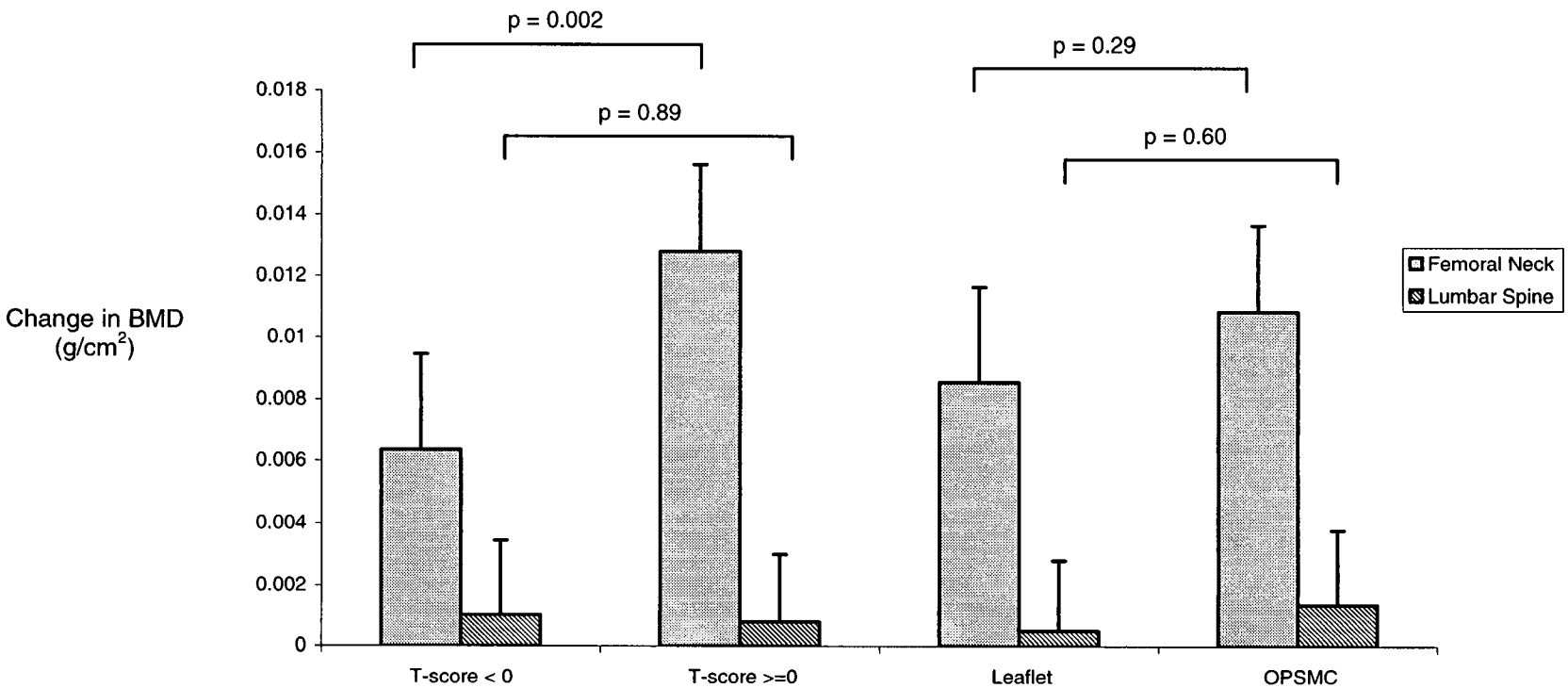


Figure 7 shows differences in osteoporosis preventive behaviours at two years by T-score group and by educational intervention. A greater proportion of subjects in the low T-score group commenced taking calcium supplements (as measured by FFQ) and reported changes in physical activity than in the high T-score group, but there were no differences between education groups. Levels of dietary calcium intake and smoking cessation were similar across both T-score and educational groups. Figure 8 demonstrates that T-score group, not educational intervention is the main determinant of commencing use of calcium supplements. There were no significant differences in changes in strenuous activity levels, average leg strength change, and change in work capacity between T-score groups or between educational groups (data not shown).

Table 18 documents the associations between changes in femoral neck and lumbar spine BMD and changes in osteoporosis preventive behaviours. In univariate analysis there were positive associations between change in femoral neck BMD and calcium supplement use (whether measured by FFQ or self-reported behaviour change) and physical activity (by self-report but not questionnaire assessment). Figure 9 shows the absolute differences in femoral neck BMD in those who did and did not change calcium supplement use and self-reported physical activity. In multivariate analysis these associations persisted. At the lumbar spine, there were no significant associations in univariate analysis. However, a positive association between change in work capacity and lumbar spine BMD change was significant in multivariate analysis.

Figure 7: Effect of intervention on change in osteoporosis preventive behaviours

(a) by T-score (b) by educational intervention

P-values are for comparison of proportion of subjects changing each behaviour between T-score groups and between educational intervention groups at two years. Significant differences in behaviour change between groups were only observed for calcium supplement use and self-reported physical activity between T-score groups. The type of educational intervention did not affect the proportion of subjects changing osteoporosis preventive behaviours.

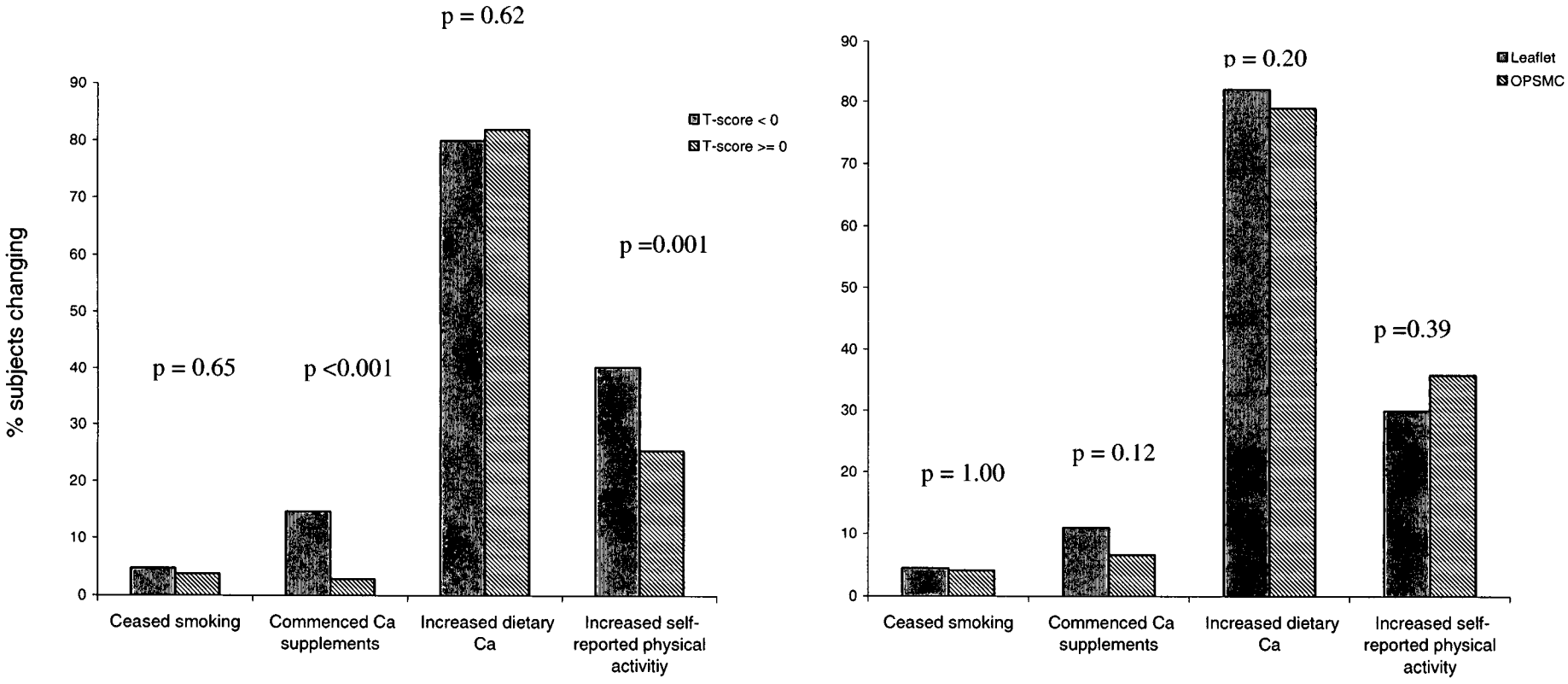

% subjects changing
90
80
70
60
50
40
30
20
10
0
T-score < 0
T-score >= 0
p = 0.62
p = 0.65
p <0.001
p =0.001
Ceased smoking
Commenced Ca supplements
Increased dietary Ca
Increased self-reported physical activitiy
Leaflet
OPSMC
p = 0.20
p = 1.00
p = 0.12
p =0.39
Ceased smoking
Commenced Ca supplements
Increased dietary Ca
Increased self-reported physical activity

Figure 8: Calcium supplement use by intervention group

This shows changes in calcium supplement use by subjects in each of the four intervention groups over the study period. Only those intervention groups that included feedback of low T-score had significant increases in calcium supplement use.

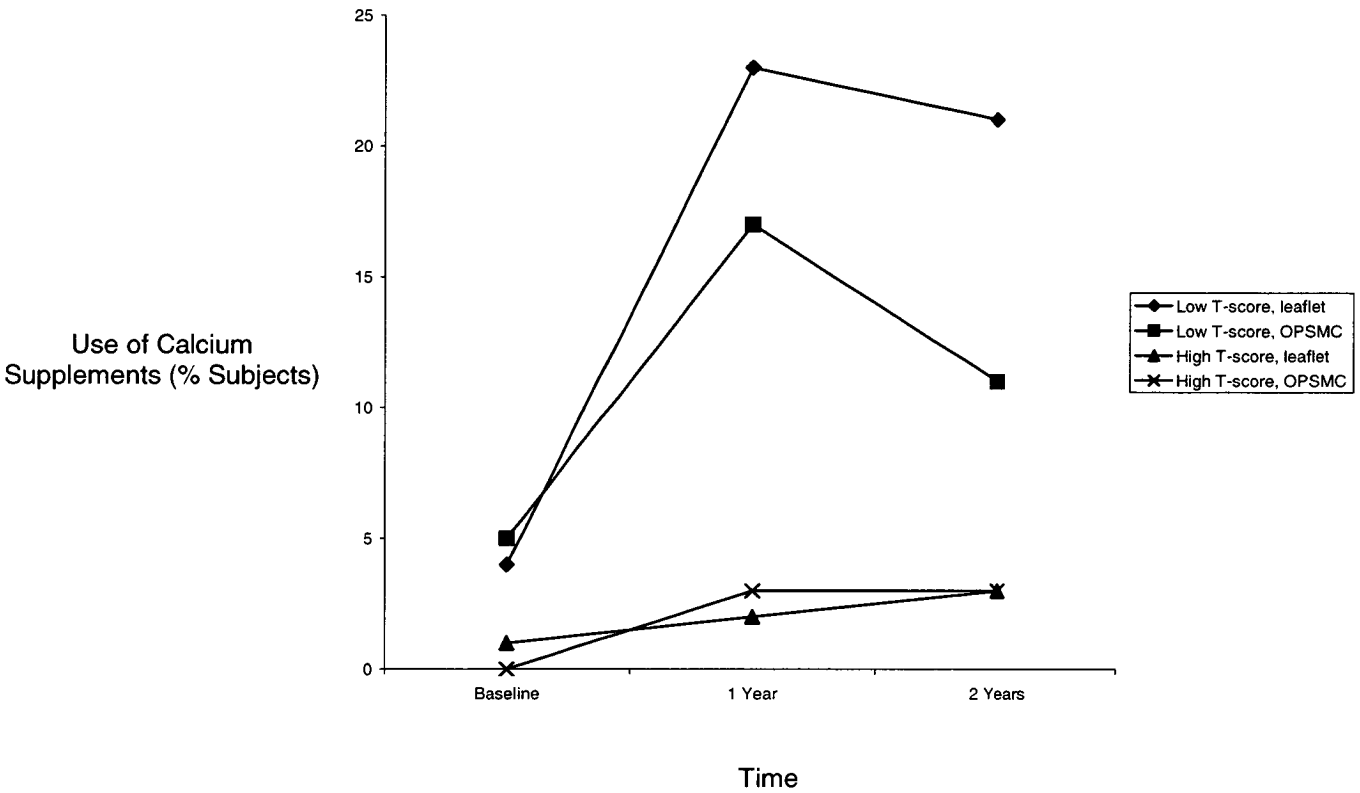
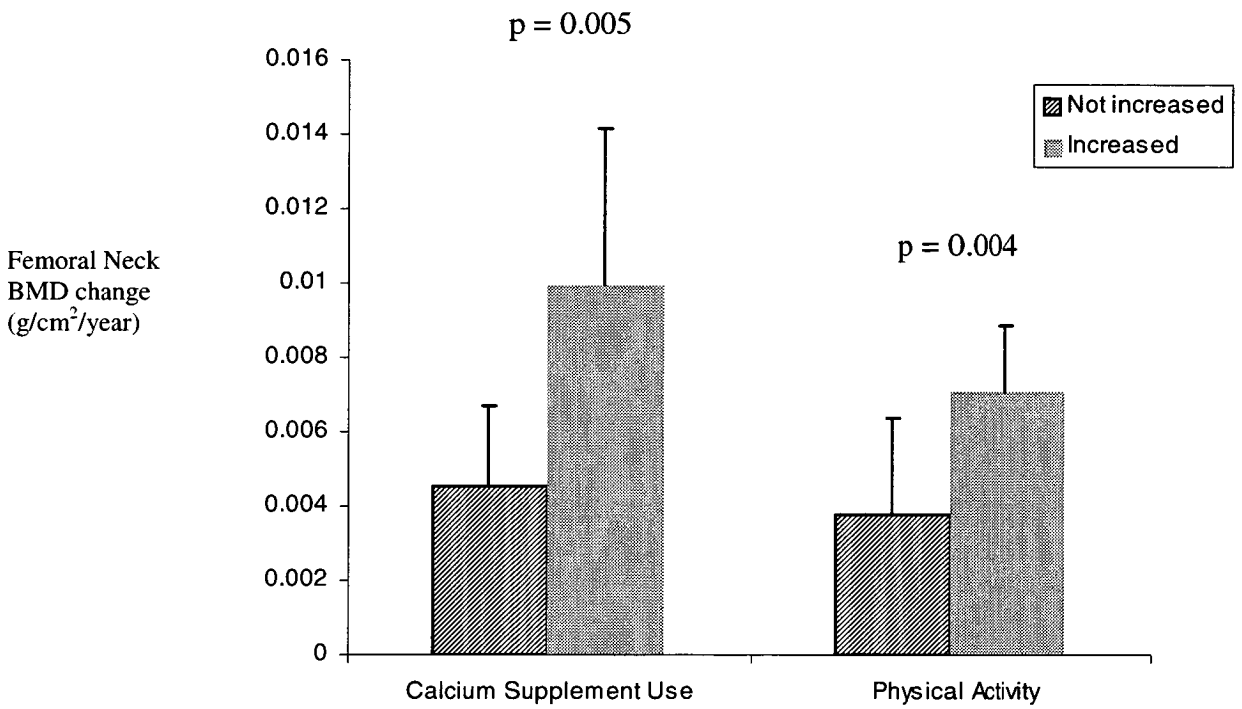


Table 18: Effect of behaviour change on BMD change

Femoral Neck BMD change (% p.a.)	Univariate β (95% CI)		Multivariate β[a] (95% CI)	
Commenced calcium supplements	**+1.37**	**(+0.54, +2.2)**	**+1.33**	**(+0.49, +2.17)**
Calcium intake change (per 100 mg)	-0.03	(-0.07, +0.02)	-0.03	(-0.08, +0.01)
Persistent smoking cessation	+0.21	(-0.9, +1.34)	-0.04	(-1.16, +1.08)
Persistent self-reported physical activity change	**+0.77**	**(+0.28, +1.3)**	**+0.72**	**(+0.22, +1.22)**
Persistent increase in strenuous activity	+0.21	(-0.35, +0.76)	+0.11	(-0.45, +0.67)
Change in work capacity (per W)	-0.10	(-0.52, +0.32)	-0.06	(-0.48, +0.36)
Change in leg strength (per SD)	+0.02	(-0.22, +0.26)	+0.02	(-0.22, +0.26)
Lumbar Spine BMD change (% p.a.)				
Commenced calcium supplements	+0.08	(-0.45, +0.62)	+0.18	(-0.37, +0.73)
Calcium intake change (per 100 mg)	0.00	(-0.03, +0.03)	-0.01	(-0.04, +0.02)
Persistent smoking cessation	+0.21	(-0.50, +0.93)	+0.11	(-0.62, +0.85)
Persistent self-reported physical activity change	-0.10	(-0.42, +0.21)	-0.05	(-0.38, +0.28)
Persistent increase in strenuous activity	-0.17	(-0.52, +0.18)	-0.16	(-0.53, +0.21)
Change in work capacity (per W)	+0.24[b]	(-0.02, +0.51)	**+0.31**	**(+0.03, +0.59)**
Change in leg strength (per SD)	+0.07	(-0.08, +0.23)	+0.05	(-0.10, +0.22)

[a]adjusted for other items in column, age, and difference in weight and height between baseline and 2 years. [b]p = 0.07

Figure 9: Mean absolute change in femoral neck BMD per year for women who did or did not increase calcium supplement use or physical activity. Data is presented as mean and upper 95th CI. P-values are for differences between women who changed and who did not change each behaviour.



All analyses were repeated after imputation of data for participants lost to follow-up (i.e. an intention to treat analysis) and the associations reported above were not altered (data not shown). The associations were unchanged also when analysis was repeated for actual OPSMC participation rather than available data analysis (Table 17) or if subjects with a baseline T-score of less than or equal to -2.5 were omitted (data not shown).

7.4 Discussion

This study demonstrates that bone density feedback with minimal patient education in premenopausal women is effective at increasing hip but not lumbar spine bone density and that this effect appears to be mediated by changes in physical activity and calcium supplement usage. However, group education had no additional effect over a simple information leaflet.

Women receiving feedback of a low T-score result were more likely to commence calcium supplement use and to report changes in physical activity, as well as to have greater increases in femoral neck BMD, compared to women with a high T-score.
Notably, the magnitude of these BMD changes, which occurred outside the setting of randomised controlled trials of interventions of calcium supplements and exercise, is similar to that obtained within such trials. Specifically, the magnitude of the effect on femoral neck BMD of self-reported physical activity change in our study was +0.7% p.a. and for calcium supplement use was +1.3 % p.a., which compared to treatment effects in premenopausal women reported for randomised controlled trials of exercise interventions of 0.9 % p.a.[66] and for calcium supplement use of 1% p.a. respectively[65]. The ability to achieve these changes with relatively simple interventions has major potential public health benefits for osteoporosis prevention and fracture reduction in later life. For example, in drug trials a change in BMD of 5% with bisphosphonates leads to a 50% decrease in fracture risk [209] while regular walking is associated with a 50% decrease in hip fracture risk [210]. The resulting behaviour changes could also be potentially beneficial for prevention of

other chronic diseases whose incidence could be reduced by increased calcium intake and/or increased physical activity, such as cardiovascular disease, obesity and diabetes mellitus.

Interestingly, the results suggest that an intervention as intensive as the OPSMC is no more effective at increasing BMD than a relatively simple and inexpensive educational intervention such as an information leaflet in this age group. The OPSMC was modeled upon a chronic disease self-management course for arthritis, which has been shown to be modestly effective in symptomatic populations at reducing health care utilisation and improving health status [173, 174]. The lack of increased effect by the addition of the OPSMC in this group of healthy, asymptomatic women is possibly due to differences in motivation between women undertaking a chronic disease self-management course who actually have a symptomatic condition, compared with a course aimed at preventing a chronic disease in healthy women. Further research is required to address the OPSMC's role in the management of other populations of women such as women with existing osteoporosis and/or fracture.

The findings that all intervention groups showed increased femoral neck BMD and that there was essentially no change in lumbar spine BMD are noteworthy given observational data for this age group. While there is no natural history data available in our geographic location, longitudinal studies examining the natural history of BMD loss in other Caucasian populations have been consistent with there being onset of bone loss in the pre-menopausal period [19, 20] with one study reporting annual loss of BMD at the femoral neck of about 0.3

% of baseline BMD p.a., and bone loss potentially beginning as early as age 24 [21]. The onset of lumbar spine bone loss was estimated at 38-39 years, with the maximum annual loss being 0.5% p.a. If premenopausal bone loss can be reduced, or potentially reversed, then this has important implications for the long-term prevention of osteoporosis and fracture. The ability to achieve this with a relatively simple intervention i.e. bone mineral density feedback with an information leaflet, has major potential public health benefits for osteoporosis prevention. However, confirmation of long-term benefits and assessment of the cost effectiveness of the intervention needs to occur before any recommendation for implementation at a population level is made.

The associations between changes in BMD and physical activity varied by site of BMD measurement, and by the physical activity measure used. Simple self-report of physical activity change was positively associated with change in femoral neck BMD, but not lumbar spine BMD. However, there was no association between changes in other physical activity measures and femoral neck BMD. Change in endurance fitness was associated with rate of change of lumbar spine but not femoral neck BMD. Changes in femoral neck BMD in exercise interventions without accompanying increases in muscle strength have been observed previously in premenopausal women [211]. Different types of exercise can also cause different BMD responses in the lumbar spine and femoral neck BMD [212, 213]. Variation in the types of activity captured by simple self-report and the site dependency of the BMD effects of different activities may account for the differences in associations seen at the lumbar spine compared to femoral neck. Alternatively, the femoral neck may be more susceptible to lifestyle interventions in premenopausal women than the lumbar spine. The difficulty of capturing all dimensions of physical activity by questionnaire is well-

known [214, 215], particularly non-leisure activities in women [216]. Simple self-report may have captured changes in incidental activity, not detected by other measures, which may have caused increases in femoral neck BMD. The use of pedometry or accelerometry to assess physical activity changes in future research may assist with elucidating the reasons behind the discrepant results.

There were no significant associations between femoral neck or lumbar spine BMD and changes in smoking habits or dietary calcium intake. The number of women who persistently ceased smoking over the study period was small (n=20), so the study had insufficient power to detect a meaningful difference in BMD. The difficulties of finding associations between calcium intake and BMD are well known [217]. The measurement error inherent in FFQ assessment of dietary intake, combined with variations between database derived nutrient contents food and actual content, and variations in the bioavailability of calcium in individuals, all make the identification of associations outside of randomised controlled trials of calcium intake problematic. In contrast, ascertainment of calcium supplement usage may have less error, thus making it easier to detect an association with calcium supplement use, as we found in this study.

This study has a number of potential limitations. While the sample was randomly selected, selection bias is possible due to the 64% response rate. The proportion of current smokers in the sample is lower than the Tasmanian prevalence of daily smoking in females aged 25-44 years in 1998 of 29% [218].However, the wide spread of education levels and the unemployment rate approximates the overall population figures for these socioeconomic factors. We have previously reported that the effects of any potential selection bias towards

a healthy cohort appear to be minor (Chapter 5) so that the results of this study are likely to be generalisable to healthy Caucasian women in the 25 to 44 year age range. Regression to the mean may account for some of the observed change in femoral neck BMD. It would not affect the associations between BMD feedback and behaviour change, nor the associations between behaviour change and BMD change. The extent of regression to the mean decreases as the correlation between pre and post intervention values increases. In this case, the correlation between baseline and follow-up femoral neck BMD was high (r=0.87) making the likelihood of regression to the mean low [219, 220]. Furthermore, if there were significant regression to the mean, we would expect to see a decrease in the high T-score group and a similar effect at the lumbar spine, which was not the case. The period of follow up for this study question is greater than that previously reported at 2 years. However, the effect of the remodeling transient which results from increased calcium intake is greatest in the 6 to 18 months after increasing calcium intake [221] so it is not possible to determine whether the effect of calcium on BMD over the two years of the study is indicative of long-term gain in steady-state bone mass or is due to the remodeling transient. Longer-term follow-up is needed to confirm any lasting positive effects on BMD from ongoing calcium supplement use. Even longer follow-up, in a much larger sample, would be needed to detect any positive effects on fracture incidence. We chose not to have an intervention group receiving BMD feedback alone without any other educational intervention. This decision was made because previous studies involving BMD feedback affecting behaviour had included leaflet information [130-132] and there was therefore an argument that supplying a minimal amount of information would be the minimum intervention that would be acceptable both practically and ethically. While this limits the ability to state categorically which effects were due to the BMD feedback and which the

leaflet, the variability between T-score subgroups suggests that BMD feedback was the more important component of the intervention. This is consistent with the results of the only randomised controlled trial of written information alone, which found no changes in behaviour from the intervention [128]. We performed additional analysis by intention to treat to assess the likelihood of loss to follow-up influencing these results, and found that the observed associations remained and were not materially different in magnitude. Lastly, to ensure the effects seen were not confounded by treatment for osteoporosis, we performed the analysis omitting the those subjects known to have been treated as well as those subjects whose T-score would have qualified them for treatment, i.e. less than -2.5 at any site. This did not substantially alter the study findings.

In conclusion, individualised BMD feedback combined with a minimal educational intervention is effective at increasing hip but not spine bone density in premenopausal women. The changes in behaviour through which this was mediated are potentially important in the prevention of other diseases, thus measuring bone density at a young age may have substantial public health benefits, particularly if these changes are sustained.

Chapter 8: A Mother-based Intervention Trial for Osteoporosis Prevention in Children.

8.1 Introduction

Low bone mineral density (BMD) is a major risk factor for osteoporotic fracture [39]. BMD in later life is a function of peak bone mass and the rate of subsequent bone loss [30] so maximizing peak bone mass is one potential way to reduce the impact of age-related bone loss. Modifiable influences on peak bone mass include nutrition, especially calcium intake [42, 222], and physical activity [44, 223-227]. There is evidence that lifestyle behaviours track from childhood to adulthood [48, 49]. Therefore, changing osteoporosis preventive behaviours in childhood may have an ongoing positive effect in adulthood, with potential to prevent fracture in later life. There is also evidence that optimizing age-appropriate bone mass has a more immediate effect as low BMD is a risk factor for fracture in childhood [45, 46, 84].

Information on how to improve osteoporosis preventive behaviours, particularly calcium intake and physical activity, in children is sparse. Two trials aimed at improving children's osteoporosis preventive behaviours have reported increased calcium intake after one year [135] and 2 years [136], but neither reported physical activity changes.

Changing lifestyle factors in children has been more often addressed in the context of the prevention and management of obesity. However, the types of interventions that are most effective remain unclear [141, 228]. One trial suggests that using parents as exclusive agents of change is more effective at reducing weight in children than intervening directly with children [143, 229]. There is also observational evidence suggesting that this parent-focused approach is worthy of further exploration [144-147]. Individualised BMD feedback combined with written information alone [131, 132] or with group-based behavioural education [230] (see

also Chapter 7), can improve osteoporosis preventive behaviour in premenopausal women. The aim of this study therefore, was to assess whether these same interventions administered to mothers have potential to influence children's behaviour, by comparing their effects on maternal-report of children's behaviour change.

8.2 Methods

See Chapter 3.

Statistics

Differences between subjects completing the study and withdrawals, and between baseline characteristics of intervention groups were assessed by oneway ANOVA and Chi-squared tests. Intention to treat analysis was performed using logistic regression to determine factors associated with maternal report of children's calcium intake and physical activity change, with both univariate and multivariate analyses, the latter adjusting for potential confounders and examining for independent effects and for interaction between T-score group and the educational intervention received. All analyses were performed in Stata version 7 (Stata Corporation, Texas, USA). Statistical significance was set as $p< 0.05$ (two-tailed).

8.3 Results

A total of 470 women (response rate 64%) were recruited. This sub-study includes the 354 women who had children. There were no statistically significant difference in baseline demographics (education level, employment status, number and age of children, family history of osteoporosis or fracture, history of fracture, smoking status and marital status) between mothers completing the study and those withdrawing except that those who withdrew were more likely to come from a household where the main financial provider was unemployed (6% vs 15%, p=0.04). There were no statistically significant differences in baseline characteristics between intervention groups (Table 19).

Ninety percent (n=320) of mothers reached final follow-up (Figure 10). Nine percent of these commenced calcium supplements themselves and 32% reported changing their level of physical activity. The proportion of mothers reporting increasing their children's calcium intake and physical activity, by T-score group and educational intervention, are given in Figure 11.

The results of analyses for predictors of women reporting changing their children's calcium intake are given in Table 20. Having a child under the age of 18 and receiving the Osteoporosis Prevention and Self-management Course were positively associated with maternal-report of change in children's calcium intake at both 1 and 2 years. Feedback of low T-score was associated with maternally-reported increases in children's calcium intake at 2 years but not at one year (Figure 11). None of these factors were associated with

maternal report of change in children's physical activity (data not shown). These results at two years were unchanged when adjusted for the mother's own self-reported behavioural change at 2 years. The associations were similar if restricted to children less than 10 years old.

There were significant associations between an increase in the child's calcium intake and commencement of calcium supplement use by the mother, and with change in the mother's self-reported physical activity. These persisted when adjusted for both maternal behaviours concurrently, though the effect of the mother commencing calcium supplements was no longer statistically significant ($p = 0.056$). However, the only maternal behaviour change associated with increase in maternally-reported children's physical activity was mother's self-reported physical activity change (OR 2.21, 95% CI 1.32, 3.72).

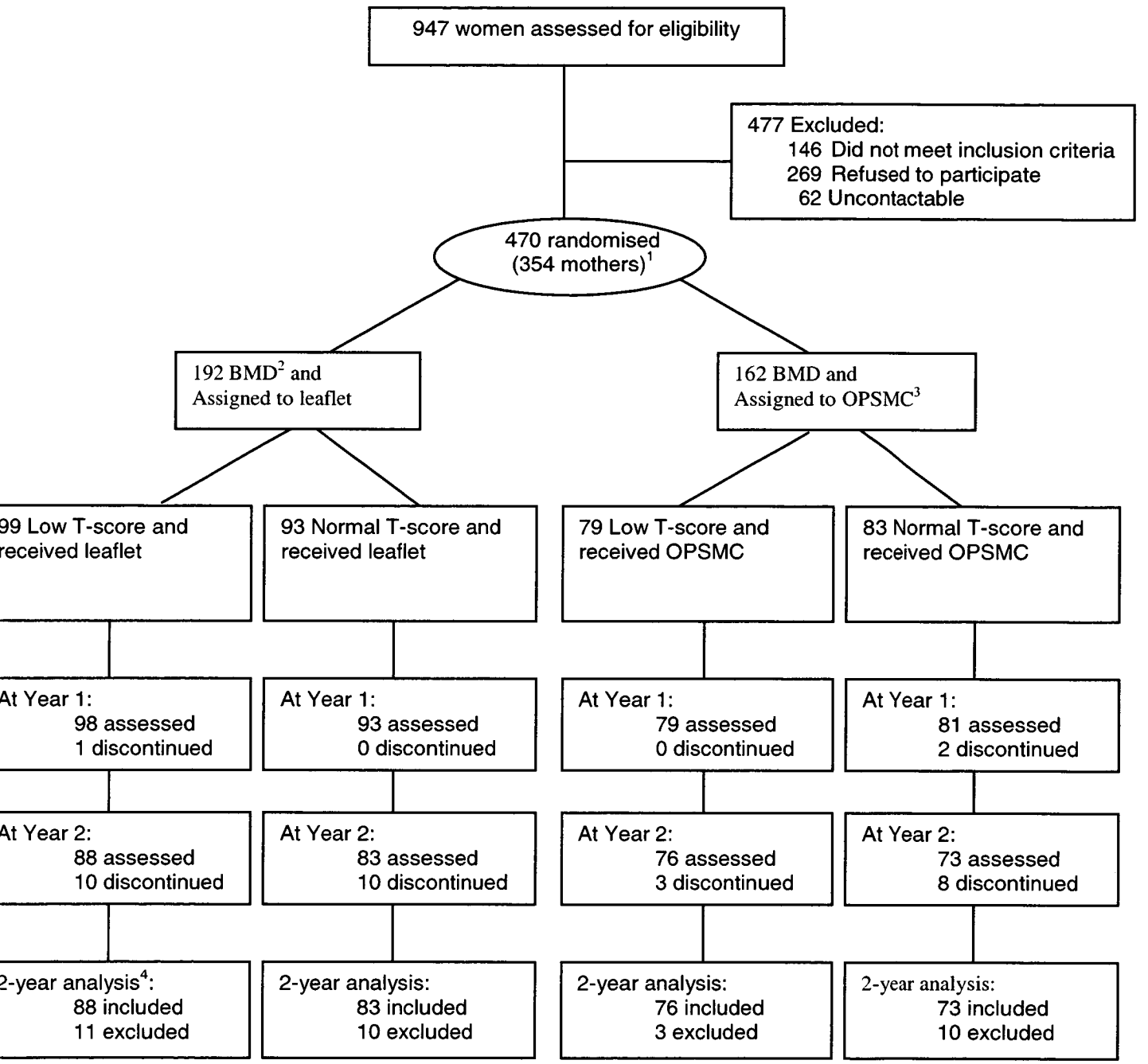
There were no associations between any change in children's behaviour and employment status of mother, family history of osteoporosis or smoking, and no interaction between t-score group and the educational intervention received (data not shown).

Table 19: Baseline characteristics of participants by intervention group in the 2000-02 study of bone mineral density feedback and leaflet vs. small group education performed in Southern Tasmania

Characteristic[a]	Group 1 T-score ≥ 0 and leaflet (n=93)	Group 2 T-score ≥ 0 and OPSMC[c] (n=83)	Group 3 T-score<0 and leaflet (n=99)	Group 4 T-score<0 and OPSMC (n=79)
Age (years)	39.7 (3.6)	39.3 (4.2)	38.9 (4.4)	39.0 (4.3)
Femoral Neck BMD[b] (g/cm^2)	1.01 (0.08)	1.03 (0.11)	0.83 (0.08)	0.83 (0.07)
Lumbar Spine BMD (g/cm^2)	1.15 (0.09)	1.18 (0.09)	0.10 (0.07)	0.99 (0.08)
Education level, %				
<Grade 10	33	50	39	33
Grade 11-12	25	12	24	20
>Grade 12	42	38	36	47
Provider unemployed,%	4	6	10	4
Employment status, %				
0 hrs/week	19	13	15	16
<20 hrs/week	27	30	32	30
>20 hrs/week	54	57	53	53
Proportion with children aged < 18 years, %	94	93	97	91
Number children, median (range)	2 (1-5)	2 (1-5)	2 (1-5)	2 (1-5)
Family history osteoporosis, %	17	8	22	15
Family history of fracture, %	58	55	60	65
Prevalent fracture(s), %	25	22	33	28
Smoking, %	17	17	17	16
Married or de facto, %	68	80	71	74

[a] mean (SD) unless otherwise stated; [b] BMD= bone mineral density, [c] OPSMC = Osteoporosis Prevention and Self-management Course

Figure 10: Flow of subjects through the trial



[1] From this point, flow diagram includes only mothers.
[2] BMD = bone mineral density
[3] OPSMC = Osteoporosis Prevention and Self-management Course
[4] Subjects were only excluded from the 2-year analysis if they had discontinued the study before 2 years of follow-up.

Table 20: Predictors of women's report of change in children's calcium intake

	Univariable Odds Ratio[a] (95% CI)[b]	Multivariable Odds Ratio[c] (95% CI)	Multivariable Odds Ratio[d] (95% CI)	Multivariable Odds Ratio[e] (95% CI)	Multivariable Odds Ratio[f] (95% CI)
Year One Follow-up					
Youngest child < 18 yrs	**4.18 (1.16, 15.09)**	**5.08 (1.27, 20.34)**			
T-score group	1.40 (0.91, 2.15)	1.46 (0.92, 2.32)			
OPSMC[b]	**2.01 (1.30, 3.12)**	**2.61 (1.63, 4.19)**			
Year Two Follow-up					
Youngest child < 18 yrs	**4.30 (1.20, 15.42)**	**5.27 (1.35, 20.56)**	**4.84 (1.24, 18.87)**	**4.62 (1.19, 17.91)**	**4.32 (1.11, 16.75)**
T-score group	**2.16 (1.38, 3.41)**	**2.20 (1.35, 3.57)**	**2.00 (1.22, 3.28)**	**2.14 (1.30, 3.51)**	**1.97 (1.19, 3.27)**
OPSMC	**1.88 (1.20, 2.95)**	**2.31 (1.41, 3.79)**	**2.40 (1.45, 3.96)**	**2.23 (1.34, 3.70)**	**2.28 (1.37, 3.80)**
Mother commenced Ca supplements (2-years)	**3.38 (1.39, 8.26)**		**3.06 (1.16, 8.04)**		2.55 (0.97, 6.72)[g]
Mother Increased physical activity	**2.70 (1.68, 4.36)**			**2.35 (1.41, 3.93)**	**2.21 (1.32, 3.72)**

[a] Bold denotes statistical significance.

[b] OPSMC =Osteoporosis Prevention and Self-management Course; 95% CI = 95% confidence interval

[c] Adjusted for having a youngest child less than 18 years old, low vs. normal T-score, receipt of leaflet vs. OPSMC, education level, marital status, family or personal history of fracture, employment status of main financial provider and age.

[d] Adjusted for having a youngest child less than 18 years old, low vs. normal T-score, receipt of leaflet vs. OPSMC, whether the mother reported commencing calcium supplement use during the study, education level, marital status, family or personal history of fracture, employment status of main financial provider and age.

[e] Adjusted for having a youngest child less than 18 years old, low vs. normal T-score, receipt of leaflet vs. OPSMC, whether the mother reported increasing her physical activity during the study, education level, marital status, family or personal history of fracture, employment status of main financial provider and age.

[f] Adjusted for having a youngest child less than 18 years old, low vs. normal T-score, receipt of leaflet vs. OPSMC, whether the mother reported increasing her physical activity during the study, whether the mother reported commencing calcium supplement use during the study, education level, marital status, family or personal history of fracture, employment status of main financial provider and age.

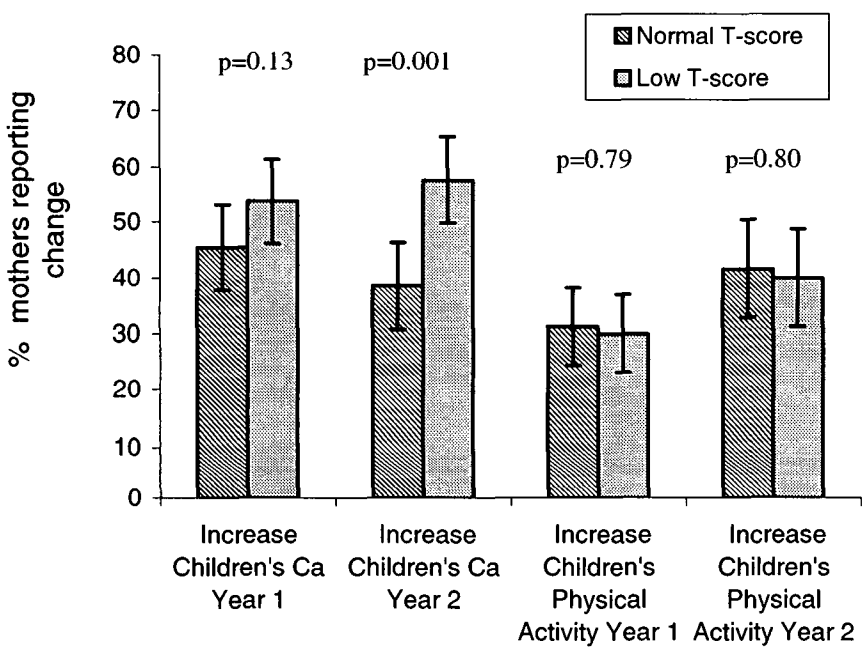
[g] p=0.05

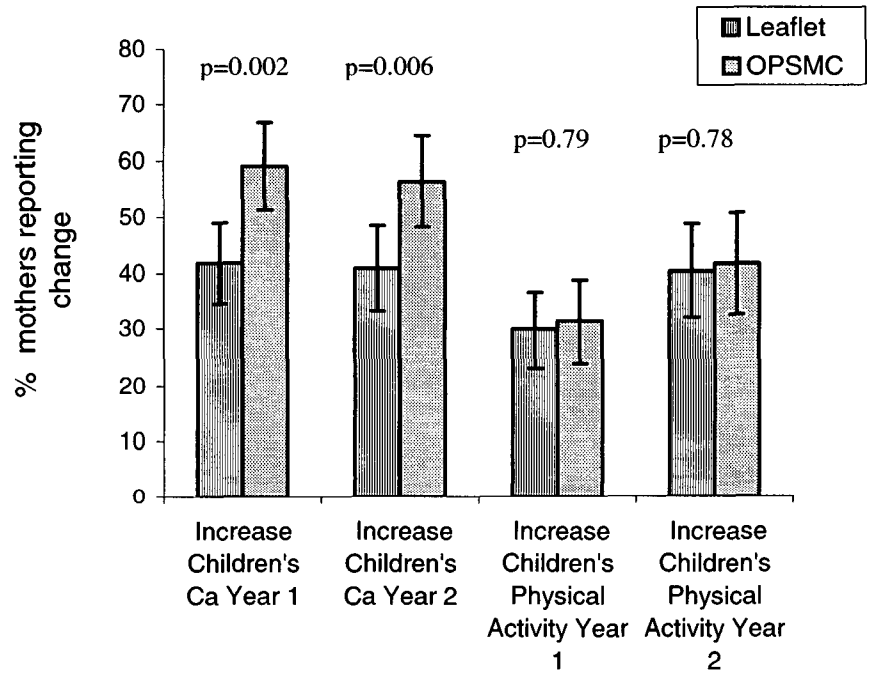
Figure 11: Maternal report of children's behaviour change by:

(a) T-score group (b) Educational intervention

Error bars show upper 95% CI.

A greater proportion of women receiving feedback of low T-score reported increasing their children's calcium intake at two years. Women receiving the Osteoporosis Prevention and Self-management Course more frequently reported increasing their children's calcium intake at both one and two years.





8.4 Discussion

The results of this study demonstrate that maternally-reported children's calcium intake and physical activity can both be influenced through their mothers. Our results provide the first evidence from a prospective trial that an exclusively parent-focused intervention may be able to improve children's physical activity, though this occurred only in those children whose mothers had changed their own physical activity behaviour. Both individualised BMD feedback and group education increase women's reporting of change in their children's calcium intake, but not their children's physical activity. Maternal behaviour change is also independently predictive of mothers reporting behaviour change in their children. While these results need to be confirmed in further studies with more objective measures of the behavioural outcomes, the maternally-reported children's behaviour changes in this study have the potential to increase bone mass and reduce fracture risk in children, as well as increase peak bone mass with its implications for long-term fracture reduction. In addition, if the behaviour changes track into adult life, there are potential benefits for the prevention of osteoporosis through reducing age-related bone loss, and for the prevention of other chronic diseases whose incidence could be reduced by increased calcium intake and/or increased physical activity, such as cardiovascular disease, obesity and diabetes mellitus.

Change in the mother's calcium supplement use and self-reported physical activity both predicted increases in children's calcium intake. However, changes in mother's physical activity but not calcium supplement use, predicted change in children's physical activity. This disparity may be partly explained by physical activity being a

more complex behaviour to change, compared to taking calcium supplements. The difficulty of changing physical activity in children is shown by the lack of success at increasing physical activity compared to calcium intake in trials specifically attempting osteoporosis preventive behaviour change [135, 136], and compared to improving eating patterns in a parent-focused childhood obesity intervention [143, 229]. Two recent reviews of interventions to promote physical activity in children [137, 138] report that even quite complex and intensive interventions did not necessarily increase physical activity. It is clear that altering physical activity behaviours may be more difficult than altering diet in children. The results of studies examining parental influences on children's physical activity are not clear-cut, with conflicting results for the influence of parental physical activity levels and parental participation with children, [147] but more consistent positive effects of direct parental help [145, 147]. Other suggested mechanisms for an association between parental and children's activity levels include modeling of physical activity by parents, sharing of activities by family members [231], parental support of children's participation [232] and genetic factors [231]. In our study, changes in physical activity in the mother may be a marker of higher levels of motivation to change, so that both physical activity and calcium behaviours are addressed in the children. Change in calcium supplement use alone perhaps demonstrates some motivation to change osteoporosis preventive behaviours, but less than that needed to accomplish physical activity change in children. Further research is needed to fully explore the reasons behind women changing their children's behaviour, and in particular to address the difficult issue of encouraging long-term increases in physical activity in children.

The effect of individualised BMD feedback on maternally-reported calcium intake change was only evident at 2 years whereas group education had an effect at 1 year. This is similar to the pattern of gains in osteoporosis knowledge in the subjects described in Chapter 6, where the OPSMC was associated with both short-term and 2-year increases in osteoporosis knowledge but feedback of low BMD was only associated with increased knowledge after 2 years [233]. This suggests that the mechanisms of both knowledge gain, and of adopting behaviour changes are different for the two interventions. The reasons why change in calcium intake but not physical activity differs between T-score groups and educational intervention groups are not clear. Intriguingly, these results contrast with the changes in the women's own behaviour, where T-score group was associated with higher levels of initiation of calcium supplement use, and a greater proportion of women increasing self-reported physical activity, and group education was not associated with changes in either behaviour (see Chapter 7). The greater likelihood of report of increased calcium intake in non-adult children reflects the greater ability of the mother to impact on young children's diet directly.

This study has several limitations. Despite the original sample being randomly selected, the mothers in the current sub-study had a lower prevalence of unemployment of the main financial provider in the household than participants withdrawing from the study. However, the wide spread of education levels and the unemployment rate approximates the overall population figures for these socioeconomic factors in those who completed the study [218]. We have previously reported that the effects of any potential selection bias towards a healthy cohort appear to be minor (Chapter 5). This study was only designed to provide a preliminary assessment of the potential of BMD feedback and

education to influence children's behaviour through their mothers, with a view to guiding further research in this area. The outcome was subjective and does not attempt to measure any gradations of activity, and there is potential for a social desirability bias in the self-report responses. However, it has been shown that parental reports of their children's activity level is associated with fitness level [234] and that parental reports of leisure time physical activity of their children differ little from those reported by the children themselves [235], so it is likely that the mother's report of changes in children's physical activity may reflect real changes. Nonetheless, the results must be interpreted with caution and it is important that further research is performed to objectively measure behaviour changes and determine the BMD effects of these changes in children.

In conclusion, both BMD feedback and small group education delivered to mothers are effective at inducing maternally-reported osteoporosis preventive behaviour change in children. While this effect is most obvious if the woman alters her own behaviour, there is an independent effect on the child regardless of behavioural change in the mother. Importantly, the results indicate that with this approach it may be possible to accomplish change in physical activity in children. These results need to be confirmed in further studies with objective measures of outcomes.

Chapter 9: How do women change osteoporosis preventive behaviours in their children?

9.1 Introduction

Information on how to specifically improve these osteoporosis preventive behaviours through lifestyle interventions in children, particularly in healthy children, is sparse. In Chapter 8, we reported on the effects of individualised BMD feedback combined with either group education or an osteoporosis information leaflet delivered to mothers on the maternal report of increase in calcium intake or physical activity in their children [236] (in press). Feedback of a low T-score result and receiving group education were both associated with maternal report of increasing calcium intake in their children. Furthermore, those women who themselves reported increasing their physical activity were also more likely to report increasing physical activity in their children. This study was limited by the fact that the reporting by mothers was in the form of yes/no questions regarding their children's behaviour change – thus the nature of the changes made and the strategies used remain unknown. However, this cohort of mothers provided a novel opportunity to explore strategies developed by mothers themselves to alter behaviour in their children, strategies which are likely to be workable in the family environment as they are likely to have evolved in response to problems encountered in everyday family situations. The aim of this study was therefore to describe the strategies and approaches used by mothers to improve calcium intake and physical activity behaviours in their children, in order to inform the development of practical and efficacious health promotion strategies in children.

9.2 Methods

9.2.1 Sample selection

We selected a sub-sample of 39 of the 354 mothers of women who completed the 2-year follow-up period of the original randomised controlled trial of individualised bone density feedback and either an osteoporosis information leaflet or group education. We used purposive sampling to ensure we selected mothers who experienced different aspects of the original intervention, and who had reported different experiences of behaviour change in their children [237]. Details of the interventions are described elsewhere [233] (see also Chapter 3). It is important to note that in both the leaflet information and in the group education there was no specific mention of how to approach lifestyle change in children. The participants had provided information about changes in their own (see Chapter 7.3) and their children's behaviour [236] (in press) (see also Chapter 8.3) two years after the bone density feedback/education interventions. Recruitment was by letter of invitation, followed by telephone contact. The study received ethics approval from the Human Research Ethics Committee (Tasmania) Network and all subjects gave written informed consent.

9.2.2 Data Collection

Mothers participated in a semi-structured interview in which they talked about their understandings of osteoporosis risk and the measures they take to prevent osteoporosis in themselves and their family members. Semi-structured interviews are an open-ended and exploratory qualitative technique where the interviewer is focused on a number of issues/questions to be explored while also allowing the conversation to flow naturally (in press)[238,239]. The interviewer uses a list of possible questions or topics (termed an interview

guide or schedule) to guide the interview. Two trained research assistants with experience in qualitative interviewing conducted the interviews. Interviews were conducted in a location selected by the interviewee. The majority were conducted in research participants' homes with the remainder occurring in a university office. The key interview questions used in our interviews were:

(1) Have you taken any measures to prevent osteoporosis in your children?

Prompts:

- why/why not?
- can you give examples? Ask participant to describe measures in detail (ask specifically about calcium/physical activity)
- ask about any measures that were easy
- ask about any measures that were difficult
- are there any measures that you are not taking that you would like to?

(2) How do you see your role in terms of preventing osteoporosis in your children?

9.2.3 Data analysis

Interviews were audio-recorded with the permission of the participant and then transcribed in full. Because the objective of the research was to identify strategies used by mothers to reduce the risk of osteoporosis for their children a simple iterative thematic method of qualitative analysis was sufficient [240]. Each transcript was read by EH and TW and coded. Coded transcripts were then re-read by TW who grouped the initial codes into broader themes related to the research objectives. At this point TW and EH reviewed the themes to ensure they accurately reflected the original interview

data. This method of iterative interpretive data analysis is derived from grounded theory [241, 242]. The data was managed using NVivo 2 software (QSR International Pty Ltd, Doncaster, Vic, Australia copyright 2003-2005). This qualitative analysis software package allowed data to be stored, searched and readily organised.

9.3 Results

We recruited 39 interviewees, from 49 attempts at contact. Two mothers were not contactable and 8 declined to participate. As expected from our use of purposive sampling, the characteristics of mothers who participated covered a range of demographics and had a range of experiences from the original trial, as shown in Table 21.

Mothers described a variety of practical and very specific dietary changes they made to increase their children's calcium intake. These included:

- changing to high calcium, low-fat milk;
- putting a extra slice of cheese in their roll;
- taking yoghurt to school;
- flavouring milk eg smoothies, milkshakes and toppings
- using drinking yoghurt instead of milk (for a child who doesn't like milk);
- high calcium soy milk (for children who won't/can't eat dairy);
- substituting for other beverages and foods e.g. "when they came home from school it used to be, you know a drink of water or you know water cordial, and [now] more often than not it's a drink of milk, like a milkshake or something like that"; "Getting them to have cereal in the mornings instead of just toast"

Mothers also described more general approaches and strategies they used to improve their children's calcium intake and physical activity, which are given in Table 22, together with illustrative quotes taken from the transcripts. The use of calcium supplementation was mentioned rarely, and usually in the context of a child with a

medical condition such as cystic fibrosis, severe allergies, milk intolerance, or history of a pituitary tumour.

Table 21: Characteristics of mothers interviewed

Characteristic	% (n=39)
Intervention received	
Low T-score feedback	51
Group education	51
Mother's behaviour change	
Commenced calcium supplement	3
Increased physical activity	38
Age of mother (years)[a]	38.5 (4.2)
Age of youngest child [a]	9.2 (4.8)
Number of children	
1	13
2	51
3	28
4 or more	8
Married or de facto	90
Education to Grade 10 or less	36
Mother working full-time	67
Main financial provider unemployed	8

[a] mean (standard deviation)

Table 22: Strategies used by mothers to improve their children's osteoporosis preventive behaviour

Theme	Typical quote
Strategies for increasing calcium intake	
(i) Raising awareness of calcium intake	"I make sure they get their 3 serves a day of dairy products" "being aware they have calcium in their diets through milk, cheese, yoghurt and increase the fish..." " I became more conscious in the calcium in their diet"
(ii) Accessibility and identifying what they like	"I always make sure ...that I get the drinking yoghurt, or something, knowing that he doesn't have huge glasses of milk..." "he loves Brie and Camembert cheese, so I buy him that..." " I know that's what he really likes, so I've had that in the fridge so he can have that when he wants it" "my daughter hates yoghurt, so trying to get her to have 3 say milkshakes and stuff" " I make sure there's plenty of sardines in the cupboard..." "I'm the one who um, buys the groceries basically cooks the meals and it's a fairly important role in terms of the food intake they have"
(iii) Role modeling	"I like the kids to see me drinking [milk], so then they know oh Mum can drink it, I can. And then when they're older like me they'll be doing the same thing"
(iv) Providing Information	"try and teach him...at his own level the importance of different things. Like he knows that it's important that you should have some milk because it's good, good for you bones...." (mother with daughter off dairy) " I say " have you had your amount of calcium this week" and she said "yes I had all my soy milk..and I had my tuna this week....""

(v) Balance in diet	"I just feed them what I think's right and healthy" "setting up really good habits, just making sure she has a good balance diet " " [osteoporosis is] something I consider with their diet....I'm not obsessive about it but if I make sure they have a good range of vegetables and dairy products...then I sort of figured they will get what they need"
(vi) Balance in approach	"I don't want to say...if you don't drink this milk you're going to get osteo, I don't do that, I don't, you know, I don't go overboard"
Strategies for increasing physical activity	
(i) Accessibility and identifying what they like	Q "was that easy to do, sort of encourage him to be more active?" R "Yeah, it's not too bad...Especially like ...if it's things like that he loves doing..." "[I say] come walking with me, but he doesn't actually like walking, so he'll come and he'll ride his bike" "walking with the dog, or opportunities, it's more to do with her friends really, and setting up activities for her to do with her friends"
(ii) Role modeling	" you set the right example yourself, so therefore um, he sees physical activities and understand the importance of it, or you pass on the enjoyment of it."
(iii) Doing things together	" I do occasionally tell her to get ...away from the computer and go for a walk, come with me" "saying things like let's go for a walk together or ...can you give me a hand, I need to get a bit fitter, come for a walk with me" "I've been able to get my daughter out, we take the dog down to the beach....you know it is so much fun watching him. I've really sucked her in, because she can't wait to get down there and watch the dog, you know"
(iv) Encourage	"I've tried to encourage her to have a bit more physical activity, walk and run, things like that."

Relevant to both calcium intake and physical activity	
(i) Accessibility and identifying what they like	Q "How do you see your role in terms of preventing osteoporosis in your kids?" R "It's just adapting my lifestyle to fit in with their lifestyle sort of thing..."
(ii) Providing Information	" ...I just think it's my job to make them aware and ...to give them information that they look after themselves. ..that's sort of a life long skill. I don't do everything for them, ...I don't think that's any help at all..." "well I explained about osteoporosis to the girls" Re role in preventing osteoporosis "mainly as an educator" "we do talk about these sort of things anyway and how important, like how your food groups and stuff like that" "I'm the instructor, ultimately I can only tell them what I can...and they need to know they are responsible"
(iii) Balanced lifestyle	"just really sort of trying to encourage a lifestyle, that they're healthy, they're active, and that sort of thing really. I sort of hope that will all, all just sort of drift down the...the chain and, and keep them well" "encouraging an active lifestyle and sensible eating habits"
(iv) Balance in approach	"Just guiding, I suppose as with anything with parenting" "often if we are driving along in the car talking...if someone will ask a question and that will lead to something else, which will lead to ...having a discussion on it, rather than saying "well you must walk to school today because otherwise, you know, this is a prevention for such and such""
(v) Age	"as they get older they listen to you more....." "when they were younger I would just go ahead and try and make sure that they had healthy food, whereas now that they ore older, then I put a little more responsibility on their shoulders..." "...he's at that age now where he has to start taking that responsibility...he's not going to be with me forever"

Mothers also discussed barriers to improving lifestyle behaviours including:

- environmental issues for physical activity such as climate issues (" I end up driving around Hobart in Winter...") and local geography ("that all comes down to where we live....being up there there's nothing unless you go for a walk..." and "it's not an area where we can walk at night");
- perceptions about high calcium foods ("the hard part was getting her mind around, well, like with foods like dairy foods and that, teenage girls, they associate fat content");
- busy lifestyles ("eating on the run some times", "you're straight to the next activity after school", "It's been hard at tea time because she works until about 7 and then we get home and she's starving hungry and wants something now, can we stop at MacDonalds...";
- family dislike of foods e.g. " I try to replace butter with tahini but even my husband said you know that's not quite normal food....and I just had to sort of maybe do it without them knowing sometimes. Like instead of actually saying I'm putting this on your sandwich... you just put it on". " I don't like milk and blah, blah blah but I just persisted and she gradually well she was having topping, like milkshakes and things";
- cost. "it costs me a fortune in fruit to feed the kids, yeah, I actually found that it's cheaper to buy chips and junk food that it is to buy fruit." "eating correctly is expensive" "it astounds me that when something is so crucial and they have big advertising campaigns saying you know children should have a drink of milk, a piece of cheese and a tub of yoghurt each day...I would imagine that people on lower incomes would find it extremely difficult..." "something a simple as the cost of a 1 kg block of regular old cheese could be out of reach of some people".

As expected, not all mothers reported making behaviour changes in their children. Those who did not reported being not concerned about osteoporosis, or that their children already had healthy diets or were very physical active and so they did not perceive osteoporosis to be a risk to their children. However, even some mothers who did not describe being concerned about osteoporosis in their children still discussed the importance of a healthy lifestyle for their children and included behaviours in this relevant to osteoporosis such as physical activity and good nutrition. Examples are given in Table 22 (themes of balanced diet and balanced lifestyle)

9.4 Discussion

This study was a unique opportunity to examine the methods used by mothers who had taken steps to improve their children's calcium intake and physical activity behaviours, in a group of mothers who had devised their own strategies without specific behavioural or other advice about how to approach intervening with their children. It therefore reflects solutions to the difficult problem of lifestyle change in children, which have arisen without preconceived ideas, and provides a unique insight into the way mothers approach this issue in their children.

Mothers identified a number of useful specific dietary changes to increases their children's dietary calcium intake. Interestingly, this usually did not include considering the use of calcium supplementation, unless children had a medical condition. Mothers did not identify any similar simple changes that were successful in increasing physical activity levels in their children. For both calcium intake behaviour and physical activity, there were a number of general strategies which came out of the interviews,

though again, these were more apparent for calcium intake than for physical activity. These strategies as well as the tips for increasing calcium intake provide useful insights into changing osteoporosis preventive behaviours in children, which can inform the development of future programs.

The strategies identified by mothers in Table 22 do not fit one particular model of behaviour change, but individual strategies are similar to concepts described in the osteoporosis preventive lifestyle change literature, though this work is predominantly in adults. For example, raising awareness of calcium intake and providing information reflect attempts to change osteoporosis knowledge, which in turn has been identified as an important contributor to exercise and calcium intake behaviour [156]. Role modeling was identified as an important strategy for increasing both calcium intake and physical activity. Role modeling is considered to be one of the four main influences on self-efficacy [168, 170], a concept which has been described as potentially one of the most important and modifiable predictors of physical activity [171] and has been reported as the strongest predictor of a health-promoting lifestyle [172]. Osteoporosis self-efficacy has been demonstrated to be an important determinant of exercise and calcium intake behaviours relevant to the prevention of osteoporosis [153, 156].

Other strategies are consistent with previous research examining influences on children's diet. Mothers describe how they identify their children's preferences for particular calcium-rich foodstuffs and ensure that the foods they like are readily accessible, which appears to be a solution to the barriers identified in previous research by children such as taste, appearance and lack of availability of appropriate food choices [243]. The comment by one mother in our study that "I'm the one who um, buys the

groceries basically cooks the meals and it's a fairly important role in terms of the food intake they have" is in fact mirrored by a comment in another study by a child "My parents buy the food...I think it's the availability of food that's around at the time..."[244] and by a similar theme in another [245]. Interestingly, in 11-12 year old children, rebellion was identified as an important factor in relation to food choice, with children disliking being "preached" to about their dietary choices [243], which in our study is reflected in the mothers' balanced approach to influencing their children's behaviour "I don't want to say...if you don't drink this milk you're going to get osteo, I don't do that, I don't, you know, I don't go overboard". Mothers' views on the barriers to improving dietary behaviours are remarkably consistent with those identified in children themselves [243-245]. In particular, children's negative perceptions about healthy foods; time pressure making it harder to access healthy foods and cost are all described by the mothers in our study as well as in the literature studying children [243-245]. This demonstrates that even without specific guidance, mothers are adept at identifying barriers to change and developing strategies to apply to changing lifestyle behaviours in their children. These results provide further support to existing observational [144-147] and trial [142, 143, 236](in press) (see also Chapter 8) evidence suggesting that a parent-focused approach is worthy of further exploration.

Mothers tended to talk more about dietary issues than physical activity in the interviews. For example, there were no simple changes described for increasing physical activity as are given above for improving calcium intake. This difference in emphasis occurred despite the interview structure being designed with an equal emphasis on dietary and physical activity changes. It is not clear whether this is due to mothers having a perception that calcium intake is more important than physical activity or because

physical activity change may have been more difficult to attempt and thus result in less discussion. Both of these are consistent with our previous observation that it was only mothers who were successful in increasing their own physical activity who were more likely to report increasing physical activity in their children, which in turn may be related to mothers' motivation levels or to perceptions of osteoporosis risk. There is other research showing the difficulty of changing physical activity in children. There is the lack of success at increasing physical activity compared to calcium intake in trials specifically attempting osteoporosis preventive behaviour change [135, 136], and compared to improving eating patterns in a parent-focused childhood obesity intervention [143, 229]. In addition, two recent reviews of interventions to promote physical activity in children [137, 138] report that even quite complex and intensive interventions did not necessarily increase physical activity. It is clear that altering physical activity behaviours may be more difficult than altering diet in children.

Mothers discussed geographical barriers such as location and climate as barriers for physical activity in their children. Other barriers more clearly identified by children themselves are reflected in the mothers' discussion of approaches to changing physical activity in their children. For example, children's preference of indoor activities such as playing on the computer [244] are dealt with under the theme of doing things together " I do occasionally tell her to get ...away from the computer and go for a walk, come with me". Other strategies described in our study such as role modeling and sharing of activities have been shown to be associated with children's physical activity levels in other studies [147, 231]. Interestingly, direct parental support is not mentioned by mothers in our study, yet has consistently been shown to have a positive effects on physical activity levels in children [145, 147 244]. It may be that mothers underestimate the

importance of the logistic support they provide to their children to support physical activity.

A common theme in the interviews was the effect of age on the responsiveness of children to their mothers' attempts to cause behaviour change. This was important in terms of the ability to produce change e.g. by directly influencing the foods eaten in the house when children were younger "when they were younger I would just go ahead and make sure they had healthy food..." but also in terms of the recognition that children would at some point be taking responsibility for their own lifestyle decisions "...he's at that age now where he has to start taking that responsibility...he's not going to be with me forever".

This study has two main limitations. Firstly, it is a purely descriptive study. There is no attempt to quantify responses. However, this open-ended, inductive methodology is ideally suited to exploring mothers' approaches to the issue of lifestyle behavioural change in their children, compared to more structured quantitative approaches such as surveys, when the survey content may reflect preconceived ideas [246, 247]. Secondly, the interviews were held with mothers who had already taken part in a lifestyle intervention themselves. It could be considered that therefore their experiences might be different from mothers who had not received any intervention. However, equally well the participation in the previous trial could simply be considered as the impetus for making changes. Parents are likely to attempt lifestyle in their children for a diversity of reasons, but the methods of accomplishing this and barriers encountered may be similar regardless of the reason for making the change. The similarity between the results of our study with the findings of other literature dealing with this issue supports this

contention. This study supplies information which can be applied to a diversity of settings.

In conclusion, this unique study shows that even without specific guidance, mothers are adept at identifying barriers to change and developing strategies to apply to changing lifestyle behaviours in their children. These results provide practical suggestions for dietary changes to include in future interventions, as well as identifying more general strategies and issues to consider when designing interventions to promote lifestyle behavioural change in children. The results also provide further support for considering parent-focused approaches to the difficult issue of improving lifestyle behaviours in children.

Chapter 10: A systematic review of calcium supplementation for improving bone density in children

10.1 Introduction

It is well accepted that childhood factors are likely to have an impact of future risk of osteoporosis [125]. As discussed in Chapter 1.2.1 and 1.2.4, maximizing peak bone mass is a potential way to minimise the impact of age-related bone loss. In addition, there is evidence that low BMD is a risk factor for fracture in childhood [45-47], suggesting that optimising age-appropriate bone mass may also have a more immediate effect on childhood fracture rates. Strategies to maximise peak bone mass in girls and boys have been identified as a priority area for research [125]. Clinical trials have shown that BMD in children can be increased by calcium supplementation [248-252] although this effect may not be maintained [250]; and by increased dairy intake [253]. Qualitative reviews have concluded that overall calcium supplementation did appear to have a favourable effect on bone outcomes [42, 222, 254]. However, there has been no quantitative systematic review of effectiveness of calcium supplementation in children, the magnitude of its effect, the duration of any effect after supplementation ends and its effect is modified by other factors.

The aims of this study are:

- To determine the effectiveness of calcium supplementation for improving bone mineral density in children;
- To determine if any effect varies by sex, pubertal stage, ethnicity or level of physical activity; and,
- To determine if any effect persists after calcium supplementation is ceased.

10.2 Methods

The protocol for this review was written à priori [255]. In this section we describe the final methods used together with reasons for any deviation from the original protocol.

10.2.1 Inclusion Criteria

The inclusion criteria for studies in the review were as follows:

(1) Types of studies

All randomised controlled trials of calcium supplementation compared with placebo, with a treatment period of at least 3 months were included. Included studies had to have areal or volumetric BMD, or bone mineral content (BMC) as an outcome, or in the case of studies using quantitative ultrasound, broadband ultrasound attenuation (BUA) and ultrasonic speed of sound (SOS).

(2) Types of participants

Trials in children (age<18 years) without co-existent medical conditions or treatments affecting bone metabolism were included.

(3) Types of interventions

Trials of calcium supplementation including supplementation by food sources. Trials of less than 3 months were excluded.

(4) Types of outcome measures

Fractures in later life would be the ideal outcome measure in intervention studies for osteoporosis prevention, however for intervention studies in children this would require following large numbers of subjects for decades and these studies have not been

performed. Therefore, in this review BMD was used as a surrogate outcome, as is commonly seen in intervention studies in children [256].

Data was extracted on areal BMD and BMC measured a minimum of 6 months after the treatment was commenced. In the original review protocol, we aimed to use percentage change from baseline, but as this was available for only a small number of studies, this was not used. The available data also did not allow for calculation of volumetric BMD as was stipulated in the original review protocol. In the case of studies using quantitative ultrasound, broadband ultrasound attenuation (BUA) and ultrasonic speed of sound (SOS) were to be used, but in the absence of studies using these measures, these outcomes were not used. The outcome measures were converted to standardized mean differences (SMD) using the Cochrane Collaboration Review Manager program (RevMan version 4.2.7). We had sufficient extractable bone measurement data for meta-analysis of the following outcomes: total body BMC, femoral neck BMD; lumbar spine BMD; distal radius BMD and upper limb BMD. Upper limb BMD included those studies included in the outcome for distal radius and additional studies with upper limb outcomes at other sites. Where multiple upper limb sites were measures, we chose the distal radius or the site closest to that point as the outcome. Methods of measurement included dual energy x-ray absorptiometry (DXA), single photon absorptiometry (SPA) and dual photon absorptiometry (DPA).

Where possible we also determined sex, age, pubertal stage, physical activity, baseline height, baseline weight, dietary calcium intake, type of calcium supplement used, ethnicity and follow-up after cessation of treatment to assess possible effect

modification by these variables. We also collected data on adverse effects, where available.

10.2.2 Search strategy for identification of studies

The search strategies included a search CENTRAL, (Cochrane Central Register of Controlled Trials) (Issue 3, 2005), MEDLINE (1966 to 1 April 2005), EMBASE (1 April 2005), CINAHL (1982 to 1 April 2005), AMED (1985 to 1 April 2005), MANTIS (1880 to 1 April 2005) ISI Web of Science (1945 to 1 April 2005), Food Science and Technology Abstracts (1969 to 1 April 2005) and Human Nutrition (1982 to 1 April 2005). Conference abstract books (Osteoporosis International, Journal of Bone and Mineral Research) were also hand searched.

For MEDLINE (OVID) the strategy used was:

1exp CALCIUM/

2exp Calcium, Dietary/

3calcium.tw.

4exp dairy products/

5dairy.tw.

6milk.tw.

7exp dietary supplements/

8or/1-7

9exp OSTEOPOROSIS/

10osteoporo$.tw.

11exp Bone Density/

12(bone adj2 loss).tw.

13(bone adj2 densit$).tw.

14bone mass.tw.

15bmd.tw.

16or/9-15

178 and 16

18limit 17 to all child <0 to 18 years>

The Dickersin filter [257] for randomised controlled trials was applied to Medline, and adapted for other databases where relevant. In the absence of evidence of publication bias we did not systematically contact content experts regarding unpublished studies. Informal contacts did not yield any unpublished studies.

10.2.3 Methods of the review

The relevant articles identified by the search strategy were independently reviewed by two reviewers (TW, KS) with initial screening of abstracts according to the inclusion criteria and with full text articles being reviewed if there was insufficient information in the abstract to assess eligibility. All data was extracted by two reviewers (TW, KS). Details regarding the study population, treatment periods, baseline demographic data and baseline and end of study outcomes were extracted independently. Differences in data extraction were resolved by referring back to the original article and establishing consensus. Each trial had a quality assessment performed independently by the same

two reviewers assessing randomisation, allocation concealment, blinding of those providing treatment and of treatment subjects, and description of withdrawals and dropouts [258, 259].

For bone density, the SMD of the endpoints at end of trial between treatment and control groups was calculated for the various outcomes. Originally, we had planned to use percentage change from baseline as the outcome measure, but this was not possible with the data available to us, and end point data was therefore used instead. Heterogeneity of the data was assessed using a Chi-square test on N-1 degrees of freedom. Meta-analysis was conducted according to a fixed effects model. If heterogeneity existed a random effects model would have been used, but this did not occur. In the absence of heterogeneity and because of limited numbers of studies for each outcome, we did not perform meta-regression and we limited our subgroup analyses to key potential effect modifiers, namely: sex; ethnicity; baseline calcium intake; pubertal status, physical activity; type of supplementation (milk extract compared to other calcium supplement forms (calcium carbonate/calcium citrate malate/calcium phosphate)) and duration of supplementation. The baseline calcium subgroups were determined by whether the baseline dietary calcium intake was less than or greater than or equal to the median value of the individual study means, which was 794 mg/day. Physical activity subgroups were chosen according to the data available in individual studies - where the studies had physical activity as a co-intervention or subgrouping, those in the low physical activity arm were included in the low physical activity subgroup for the review and those in the high physical activity arm in the high physical activity subgroup for the review. For study duration, we initially chose a cut-off of 24 months duration so as to sure of exceeding any period of rapid change from

the bone remodeling transient. Because this left few studies in the longer duration subgroup, we repeated the analysis using an 18-month cut-off, which is likely to still have exceeded the time needed for the effects on bone of remodeling changes to appear and a new steady state to be reached. We also performed a subgroup analysis whether the calcium intake in the intervention group in the trial exceeded the probable threshold below which skeletal accumulation varies with intake and above which skeletal accumulation appears constant regardless of intake [260, 261]. This was an analysis additional to those specified in the original protocol.

Where necessary the authors of the primary studies were contacted to obtain additional information. We aimed to use intention-to-treat data from the individual clinical trials wherever possible. If this data was not available, we used data from available treatment analysis. If no other data were available we used data from treatment received analysis. For the single study [262] in which upper limb outcomes were presented as percent change from baseline, and no endpoint data could be obtained from the authors, we imputed endpoint data using the formula endpoint BMD= (100% +%change) x baseline BMD and assumed the endpoint standard deviation (SD) was the same as that seen at baseline (as was observed in other studies for upper limb outcomes). Where studies reported the outcome as absolute change from baseline and endpoint data were not available [249, 252, 263-265] we imputed the endpoint using (baseline plus change) for the mean in both treatment and control arms, and using the standard deviation of the baseline data for the endpoint SD.

Funnel plots were performed for assessment of publication bias.

Our method of imputing the standard deviation for studies which gave change rather than endpoint data was likely to result in those studies being given more rather than less weight. We therefore performed a sensitivity analysis for the main effects omitting studies for which data was imputed [249, 252, 262-265]. We also performed a sensitivity analysis omitting the study [252] that used treatment received rather than intention to treat or available data analysis. In the absence of heterogeneity, sensitivity analyses were not performed to assess the impact of study quality on results.

We used the grading system described in the 2004 book Evidence-based Rheumatology [266] to grade the evidence in this review.

10.2.4 Clinical relevance

The SMD effect size was used to estimate an absolute benefit in mg/cm2 by estimating the pooled SD from the means of the SD of the outcomes in treatment and control groups for each study, and multiplying the SMD by this [267]. Relative difference in the change from baseline was estimated as the absolute benefit divided by the mean of all the baseline means of the control groups, expressed as a percentage. The result of this analysis is reported in the text of the review results and discussion.

10.3 Results

10.3.1 Description of studies

We identified 233 references to potential studies. Of these, 155 were excluded as they were not randomised controlled trials. Of the remaining 78 references, 9 were to trials without calcium supplementation as an intervention, 7 were to trials in participants with conditions predisposing to osteoporosis and 3 were to studies in adults. Of the remaining 59 references to RCTs of calcium supplementation in children, the following references were excluded for the following reasons:

- 16 references were to studies with either no placebo [253, 268-281] or which used an active placebo [282]
- 3 were duplicate publications [283-285]
- 2 did not measure BMD or BMC or ultrasound measures of bone as outcomes [286, 287]
- 1 included vitamin D with calcium as the intervention [288]
- 1 had inadequate randomisation [289]
- 1 had outcomes measured after< 6 months follow-up [290]

References to excluded references are found in Appendix 7 and reasons for each exclusion in Appendix 8.

The remaining 35 references to 19 studies were included in the systematic review, and each reference to the 19 included studies is given in Table 23.

Additional data was requested from authors of 8 eligible studies, of whom 5 supplied the additional information sought [248, 291-294]. In only one of the cases where additional

information was not obtained, did this result in no usable data being available for the meta-analysis [295]. All other eligible studies provided useful data for pooling.

The 19 RCTs included a total of 2859 participants, of whom 1367 were randomised to receive calcium supplementation, 1426 were randomised to placebo, and 66 withdrew from the study and the intervention group to which they were randomised was not stated. Table 23 summarises the characteristics of these studies. No studies used ultrasound measures of bone outcomes. One study used intention-to-treat analysis [296]; in one study the type of analysis was not stated [295]; in one study [252] only data from treatment received analysis was available for the femoral neck, lumbar spine and upper limb BMD at end of the trial. The remaining studies used available data analysis. Five studies had loss to follow-up of less than 5% [250, 262, 292, 296, 297], 5 had a loss to follow-up of between 5 and 20% [249, 252, 264, 293, 298] and 8 had loss to follow-up of more than 20% [248, 251, 263, 265, 291, 294, 299, 300] of their trial participants. One study did not report withdrawals and drop outs [295]. Three studies had physical activity as a co-intervention [264, 292, 293] and one had physical activity subgroups of exercise (7.2 hours exercise per week) and sedentary (1.2 hours exercise per week) [294].

10.3.2 Methodological quality of included studies

Two reviewers independently rated the methodological quality of each eligible study. Any disagreement was resolved by consensus, with the third reviewer not being required to contribute for these to be resolved. Adequate description of randomisation was given for 4 studies [264, 292, 294, 296], the remaining studies were stated to be randomised but randomisation procedures were not described. Four studies [252, 293, 294, 296] described adequate allocation concealment, the description in the remainder of the studies was

unclear. Adequate description of blinding of subjects was given in all studies except 2 [263, 265] in which the description was unclear, though all were controlled with adequate placebo. Thirteen studies gave an adequate description of withdrawals and drop outs [248-252, 263, 265, 291, 292, 294, 296, 297, 300] and 6 did not [262, 264, 293, 295, 298, 299]. Overall, the risk of bias was rated as low in 2 studies [294, 296], moderate in 12 studies [248-252, 263, 265, 291, 292, 295, 297, 300], and high in 5 studies [262, 264, 293, 298, 299].

Table 23: Characteristics of included studies, showing all references to each study.

Study	Supplement type[a], Ca (mg/day)	Duration (yrs)	N[b]	Ethnicity/pubertal stage	Female, %	Age, Mean (Range) (yrs)	Baseline Ca (mg/day)	Sites Measured
Bonjour 1995 [252, 301-304]	Milk extract, 850	Supplement: 1 Follow-up: 8	149	White/prepubertal	100	7.93 (6.6-9.4)	752	Radius, hip, LS
Cameron 2004 [291]	$CaCO_3$, 1200	Supplement: 2 Follow-up: 2	128	Unknown/prepubertal	100	10.3 (8-13)	716	Hip, forearm, LS, TB
Chevalley 2005 [263]	Milk extract, 850	Supplement: 1 Follow-up: 2	235	White/prepubertal	0	7.44 (6.5-8.5)	752	Radius, hip, LS, TB
Courteix 2005 [294]	$CaPO_4$, 800	Supplement: 1 Follow-up: 1	113	White/prepubertal	100	9.91 (8-13)	994	Radius, hip, LS , TB
Dibba 2000 [296, 305]	$CaCO_3$1000mg 5 days/ week	Supplement: 1 Follow-up: 3	160	Gambian/mixed	50	10.3 (8.3-11.9)	338	Radius
Iuliano-Burns 2003 [264]	Foods fortified by milk minerals, 400	Supplement: 0.7 Follow-up: 0.7	72	Asian 15%, 85% n.s.[c]/mixed	100	8.86 (7-11)	674	TB, upper &lower limb, LS

Johnston 1992 [248, 306, 307]	CaCM, 1000mg	Supplement: 3 Follow-up: 6	140	White/ mixed	61	10 (6-14)	919	Radius, hip, LS
Lee 1994 [250, 308]	$CaCO_3$, 300	Supplement: 1.5 Follow-up: 2.5	163	Chinese/prepubertal	46	7.18 (n.s.)	277	Radius
Lee 1995 [251, 309]	$CaCO_3$, 300	Supplement: 1.5 Follow-up: 3	109	Chinese/prepubertal	43	n.s (7 year olds)	567	Radius, hip, LS
Lloyd 1993 [249, 310-312]	CaCM, 500	Supplement: 2 Follow-up: 2	112	White/mixed	100	11.9 (n.s.)	976	Pelvis, LS, TB
Matkovic 2004 [299, 313-315]	CaCM, 1000	Supplement: 7 Follow-up: 7	354	White/peripubertal	100	10.8 (n.s.)	837	Radius, TB
Molgaard 2004 [297]	$CaCO_3$, 300	Supplement: 1 Follow-up: 2	113	White/mixed	100	13.2 (12-14)	841	TB
Nowson 1997 [300]	$CaCO_3$/Ca lactate gluconate, 1000	Supplement: 1.5 Follow-up: 1.5	110	n.s/mixed	100	14 (10-17)	734	Forearm, hip, LS, TB

Prentice 2005 [292]	$CaCO_3$, 1000	Supplement: 1 Follow-up: 1	150	White/post-pubertal	0	16.8 (16-18	1198	Radius, hip, TB
Rodda 2004 [295]	$CaCO_3$, 1200	Supplement: 1-4 Follow-up: 4	93	Chinese 43%/white 57%/n.s	100	N.S. (10-12)	n.s.	TB, LS
Rozen 2003 [298, 316]	$CaCO_3$, 1000	Supplement: 1 Follow-up: 4.5	112	Jewish 76%, arab 24%/post pubertal	100	14.85 (12-17)	582	Hip, LS, TB.
Specker 2003 [265]	$CaCO_3$, 1000	Supplement: 1 Follow-up: 1	239	White/prepubertal	47	3.92 (3-5)	946	TB, arm, leg
Stear 2003 [293]	$CaCO_3$, 1000	Supplement: 1.3 Follow-up: 1.3	144	n.s./ post pubertal	100	17.3 (16-18)	938	Radius, hip, LS, TB.
Wang 1996 [262]	$CaCO_3$, 300	Supplement: 1.5 Follow-up: 1.5	163	Chinese/prepubertal	46	7.2 (N.S.)	277	Radius

[a] $CaCO_3$ = calcium carbonate, Ca = calcium, CaCM= calcium citrate malate, $CaPO_4$= calcium phosphate

[b] number of subjects randomised

[c] n.s. = not stated

10.3.3 Results of the review

Table 24 give the treatment effects, as standardised mean differences (SMD) at each site at the end of the period of calcium supplementation and the results at the longest period of follow-up available after calcium supplementation was ceased for each trial. There was no effect of calcium supplementation on BMD at the femoral neck (+0.07, 95%CI-0.05, +0.19) or lumbar spine BMD (+0.08, 95% CI -0.04, +0.20). There was a small effect on upper limb BMD (+0.14, 95%CI +0.04, +0.24) (Figure 12 a) and total body BMC (+0.14, 95% CI+0.01, +0.27) (Figure 13) and which persisted after supplementation ceased only in the upper limb (+0.14, 95%CI+0.01, +0.28) (Figure 12 b). This is approximately equivalent to a treatment effect of 6.38 mg/cm^2 or an approximately 1.8% greater increase in supplemented groups over the course of supplementation; and to a 6.30 mg/cm^2 or 1.8% greater increase after follow-up after supplementation had ceased. A single study [298] reported on total body BMC after cessation of supplementation, and this showed no persistent effect (SMD 0.0, 95%CI -0.40, +0.40). There was no significant heterogeneity for the results at any site ($p= 0.29$ to $p>0.99$).

Table 24: Main effects of calcium supplementation at different sites

Site	Effects at end of trial			Effects after supplementation ceased		
	No. studies	No. participants	Effect size[a]	No. studies	No. participants	Effect size
Femoral neck BMD (g/cm^2)	10	1073	+0.07 (-0.05, +0.19)	5	617	+0.10 (-0.06, +0.26)
Lumbar spine BMD (g/cm^2)	11	1164	+0.08 (-0.04, +0.20)	5	617	-0.01 (-0.16, +0.17)
Total body BMC (g)	9	953	**+0.14 (+0.01, +0.27)**	1	96	0.00 (-0.40, +0.40)[b]
Upper limb BMD (g/cm^2)	12	1579	**+0.14 (+0.04, +0.24)**	6	840	**+0.14 (+0.01, 0.28)**

[a] standardised mean difference (SMD) (95% CI); an SMD of 0.3 is regarded as small[317].

[b] single study only

Figure 12 (a): Effect of calcium supplementation in the upper limb at the end of trial.

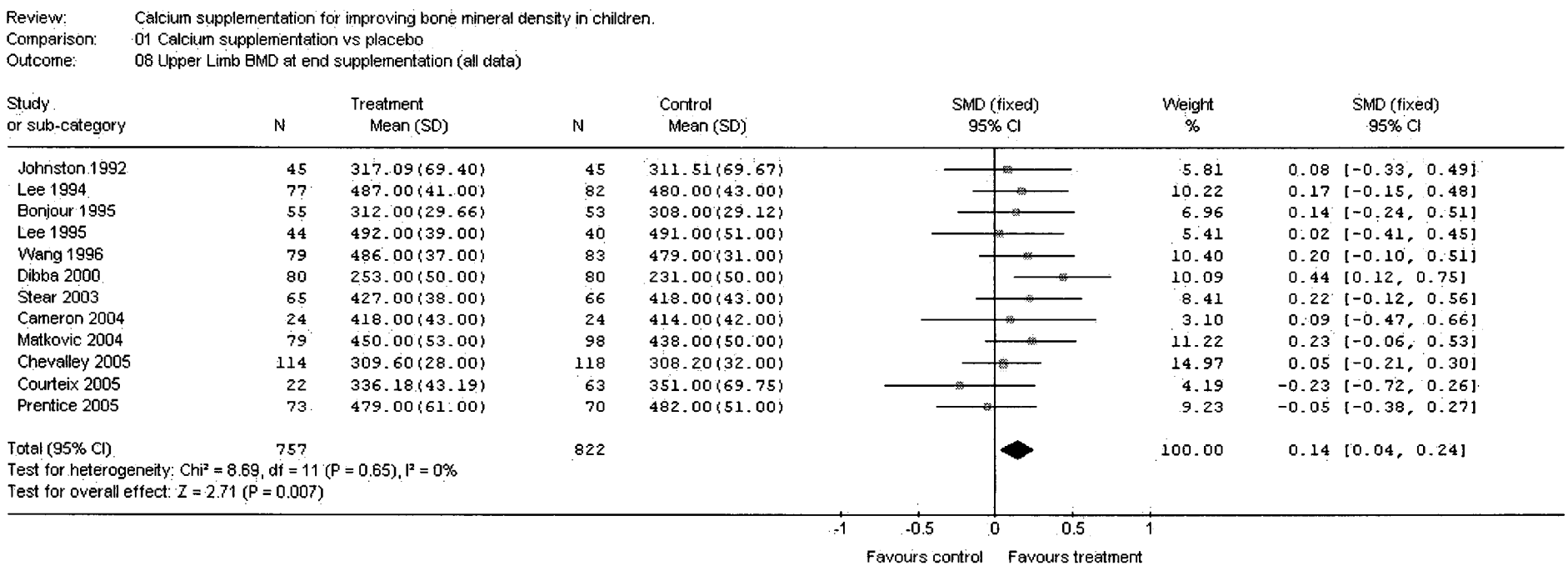


Figure 12 (b): Effect of calcium supplementation in the upper limb at the longest point after supplementation ceased.

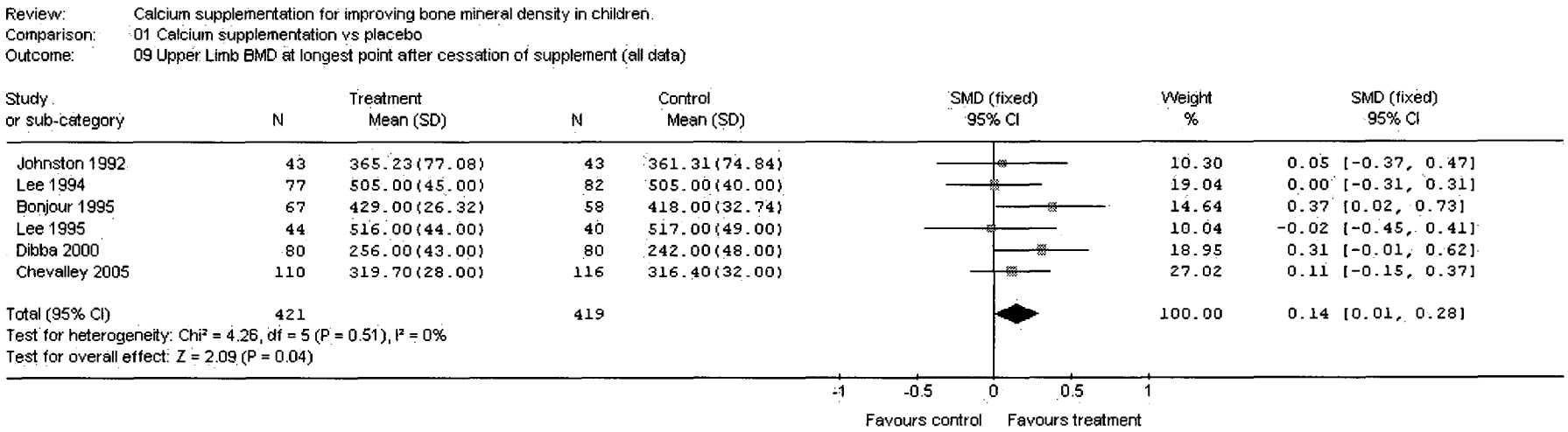
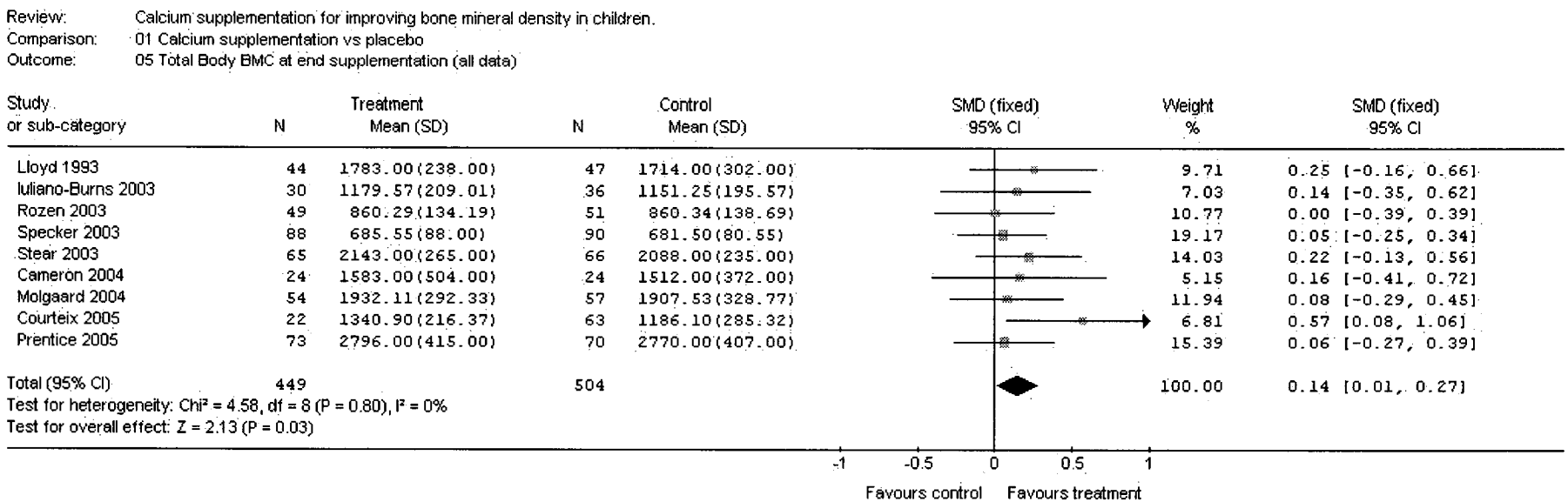


Figure 13: Effect of calcium supplementation on total body BMC at the end of trial.



Subgroup analyses by baseline calcium intake, sex, ethnicity, physical activity, pubertal stage, type of supplementation (milk extract or other), duration of supplementation and by whether the calcium threshold was exceeded all did not demonstrate significant effect modification at any site (Tables 25-33). Point estimates of treatment effects during supplementation were greater at all sites in females than males (Table 26), though these differences were not significant. At the upper limb, treatment effects during supplementation were similar in magnitude and not significant in both Caucasian and Chinese population studies but a relatively strong effect was seen in the single study in an African population (+0.44, 95%CI +0.12, +0.75). A single study described a gain in lumbar spine BMD of 0.045 g/cm^2 in Chinese but not Anglo-Celt girls [295] but the study provided insufficient data to be included in the meta-analysis. Subgroup analysis by physical activity level, showed no evidence of effect modification though there were only two studies with extractable data for the femoral neck, lumbar spine and upper limb outcomes. One study not included in the meta-analysis demonstrated interaction between calcium supplementation and physical activity using femoral BMC as an outcome but not for tibia-fibula BMC [264].

Numbers of studies available for subgroup analyses were limited for some outcomes. Only a single study [298] measured TB BMC after supplementation ceased so subgroup analyses for this outcome were not possible. Only one study reported TB BMC for males [292] and only one reported femoral neck and lumbar spine BMD after supplementation ceased for males [263]. Only one study described results in purely peri-pubertal children [299] and there were insufficient data for any subgroup analysis by pubertal stage for effects after cessation of supplementation. No studies in Chinese

populations had total body BMC data, and only a single study using milk extract as a supplement had total body BMC data.

Funnel plots for each outcome did not suggest the presence of publication bias (data not shown).

Sensitivity analyses omitting results only given from active treatment analysis did not substantially alter the results of the review. Omitting the studies with imputed values reduced the effect at the upper limb after cessation of supplementation from an SMD of +0.14 (95%CI+0.01, +0.28) to +0.10 (95% CI -0.07, +0.28) and marginally widened the confidence interval around the effect on total body BMC at the end of supplementation (+0.15, 95%CI -0.01, +0.31) without changing the size of the point estimate of the treatment effect. Sensitivity analyses did not substantially affect the review results for any other outcomes.

Adverse events were reported infrequently and were minor in nature.

The evidence in this review is graded as gold [266].

Table 25: Effect by baseline calcium intake[a]

Site	Low calcium			High Calcium		
	No. studies	N[b]	SMD (95% CI)[c]	No. studies	N	SMD (95% CI)
Effect at end of trial						
Femoral neck BMD (g/cm^2)	5	516	-0.02 (-0.19, +0.16)	5	557	+0.15 (-0.02, +0.32)
Lumbar spine BMD (g/cm^2)	5	516	+0.03 (-0.14, +0.21)	6	648	+0.12 (-0.04, +0.28)
Total body BMC (g)	4	265	+0.11 (-0.13, +0.35)	6	688	**+0.15 (+0.00, +0.31)**
Upper limb BMD (g/cm^2)	6	845	**+0.17 (+0.04, +0.31)**	6	734	+0.10 (-0.05, +0.24)[d]
Effect at end of follow-up after supplement ceased						
Femoral neck BMD (g/cm^2)	3	406	+0.02 (-0.18, +0.21)	2	211	+0.27 (-0.01, +0.54)
Lumbar spine BMD (g/cm^2)	3	406	-0.02 (-0.21, +0.18)	2	211	+0.06 (-0.21, +0.33)
Upper limb BMD (g/cm^2)	4	629	**+0.17 (+0.01, +0.32)**	2	211	+0.24 (-0.03, +0.51)[e]

[a] calcium subgroups divided by median of mean baseline intake of studies, cut point 794 mg/day; [b] N = number of participants

[c] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317].

[d] p=0.06; [e] p=0.08

Table 26: Effects by sex

Site	Males			Females		
	No. studies	N[a]	SMD (95% CI)[b]	No. studies	N	SMD (95% CI)
At end supplementation						
Femoral neck BMD (g/cm^2)	2	375	-0.05 (-0.26, +0.15)	6	524	**+0.19 (0.02, +0.37)**
Lumbar spine BMD (g/cm^2)	2	375	+0.06 (-0.14, +0.26)	7	615	+0.11 (-0.05, +0.27)
Total body BMC (g)	1	143	+0.06 (-0.27, +0.39)	7	632	**+0.18 (+0.02, +0.34)**
Upper limb BMD (g/cm^2)	3	459	+0.03 (-0.15, +0.21)	6	624	+0.15 (-0.01, +0.31)[2]
After withdrawal of supplementation						
Femoral neck BMD (g/cm^2)	1	226	-0.03 (-0.29, +0.23)	2	221	**+0.31 (+0.04, +0.58)**
Lumbar spine BMD (g/cm^2)	1	226	+0.05 (-0.22, +0.31)	2	221	+0.04 (-0.22, +0.31)
Upper limb BMD (g/cm^2)	2	310	+0.14 (-0.08, +0.37)	2	200	**+0.30 (+0.02, +0.58)**

[a] N = number of participants

[b] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317].

Table 27: Effect by pubertal stage[a]

Site	Pre-pubertal			Post-pubertal			Peripubertal[d]		
	No. studies	N[b]	SMD (95% CI)[c]	No. studies	N	SMD (95% CI)	No. studies	N	SMD (95% CI)
Effect at end of trial[b]									
Femoral neck BMD (g/cm^2)	5	557	+0.07 (-0.10, +0.24)	2	274	+0.10 (-0.14, +0.34)	0	-	-
Lumbar spine BMD (g/cm^2)	5	557	-0.06 (-0.10, +0.23)	2	274	+0.11 (-0.12, +0.35)	0	-	-
Upper limb BMD (g/cm^2)	7	898	**+0.09 (-0.05, +0.22)**	2	274	+0.08 (-0.16, +0.31)	1	177	+0.23 (-0.06, +0.53)

[a] there were insufficient data at any site for this subgroup analysis for outcomes from follow-up after supplementation ceased.

[b] N = number of participants

[c] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317].

[d] only one study reported results for peripubertal children

Table 28: Effect by ethnicity

Site	Caucasian			Chinese			Other ethnic group		
	No. studies	N[a]	SMD (95% CI)[b]	No. studies	N	SMD (95% CI)	No. studies	N	SMD (95% CI)
Effect at end of trial									
Femoral neck BMD (g/cm^2)	5	658	+0.05 (-0.10, +0.21)	1	84	-0.01 (-0.44, +0.41)	1	96	+0.09 (-0.31, + 0.49)
Lumbar spine BMD (g/cm^2)	6	749	+0.09 (-0.06, +0.24)	1	84	+0.03 (-0.39, +0.46)	1	96	0.00 (-0.40, +0.40)
Total body BMC (g)	5	608	+0.14 (-0.02, +0.31)[c]	0	0	-	1	100	0.00 (-0.39, +0.39)
Upper limb BMD (g/cm^2)	6	835	+0.06 (-0.08, +0.2)	3	405	+0.15 (-0.04, +0.35)	1	160	**+0.44 (+0.12, +0.75)**
Effect at end of follow-up after supplement ceased									
Femoral neck BMD (g/cm^2)	3	437	+0.11 (-0.08, +0.30)	1	84	0.00 (-0.43, +0.43)	1	96	+0.14 (-0.26, +0.54)
Lumbar spine BMD (g/cm^2)	3	437	+0.05 (-0.13, +0.24)	1	84	-0.20 (-0.63, +0.23)	1	96	0.00 (-0.40, +0.40)
Upper limb BMD (g/cm^2)	3	437	**+0.25 (+0.06, +0.44)**	2	243	-0.01 (-0.26, +0.24)	1	160	+0.31 (-0.01, +0.62)[d]

[a] N = number of participants; [b] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317]. [c] p=0.08; [d] p=0.05

Table 29: Effect by physical activity level[a,b]

Site	High physical activity			Low physical activity		
	No. studies	N[c]	SMD (95% CI)[d]	No. studies	N	SMD (95% CI)
Effect at end of trial						
Femoral neck BMD (g/cm^2)	2	129	+0.24 (-0.14, +0.61)	2	87	+0.29 (-0.15, +0.73)
Lumbar spine BMD (g/cm^2)	2	129	+0.07 (-0.30, +0.45)	2	87	+0.23 (-0.21, +0.67)
Total body BMC (g)	4	254	+0.22 (-0.04, +0.48)[e]	4	209	+0.13 (-0.14, +0.41)
Upper limb BMD (g/cm^2)	2	129	-0.06 (-0.43, +0.31)	2	87	+0.34 (-0.10, +0.78)

[a] high physical activity was defined as defined in the original study's subgrouping or as the intervention group where exercise was a co-intervention; low physical activity was defined as defined in the original study's subgrouping or as the control group where exercise was a co-intervention. [b] there were insufficient data at any site for this subgroup analysis for outcomes from follow-up after supplementation ceased. [c] N = number of participants; [d] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317]. [e] p =0.09

Table 30: Effect by duration of supplementation (< 24 months vs. >= 24 months)

Site	Duration < 24 months			Duration >= 24 months		
	No. studies	N[a]	SMD (95% CI)[b]	No. studies	N	SMD (95% CI)
Effect at end of trial						
Femoral neck BMD (g/cm^2)	8	935	+0.08 (-0.05, +0.21)	2	138	-0.03 (-0.36, +0.30)
Lumbar spine BMD (g/cm^2)	8	935	+0.07 (-0.06, +0.20)	3	229	+0.11 (-0.15, +0.37)
Total body BMC (g)	7	814	+0.13 (-0.01, +0.27)	2	139	+0.22 (-0.12, +0.55)
Upper limb BMD (g/cm^2)	9	1264	**+0.13 (+0.02, +0.24)**	3	315	+0.17 (-0.06, +0.39)
Effect at end of follow-up after supplement ceased						
Femoral neck BMD (g/cm^2)	4	531	+0.11 (-0.06, +0.28)	1	86	+0.01 (-0.41, +0.44)
Lumbar spine BMD (g/cm^2)	4	531	-0.01 (-0.16, +0.18)	1	86	+0.05 (-0.38, +0.47)
Upper limb BMD (g/cm^2)	5	754	**+0.20 (+0.06, +0.34)**	1	86	+0.05 (-0.37, +0.47)

[a] N = number of participants

[b] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317]

Table 31: Effect by duration of supplementation (< 18 months vs. >= 18 months)

Site	Duration < 18 months			Duration >= 18 months		
	No. studies	N[a]	SMD (95% CI)[b]	No. studies	N	SMD (95% CI)
Effect at end of trial						
Femoral neck BMD (g/cm^2)	6	793	+0.10 (-0.05, +0.24)	4	278	-0.01 (-0.24, +0.23)
Lumbar spine BMD (g/cm^2)	6	793	+0.08 (-0.07, +0.22)	5	369	+0.09 (-0.11, +0.30)
Total body BMC (g)	7	814	+0.13 (-0.01, +0.27)[c]	2	139	+0.22 (-0.12, +0.55)
Upper limb BMD (g/cm^2)	6	859	+0.12 (+0.02, +0.26)[c]	6	720	**+0.16 (+0.01, +0.30)**
Effect at end of follow-up after supplement ceased						
Femoral neck BMD (g/cm^2)	3	447	+0.14 (-0.05, +0.32)	2	170	+0.01 (-0.29, +0.31)
Lumbar spine BMD (g/cm^2)	3	447	+0.04 (-0.14, +0.23)	2	170	-0.07 (-0.38, +0.23)
Upper limb BMD (g/cm^2)	3	511	**+0.30 (+0.13, +0.48)**	3	329	+0.01 (-0.21, +0.22)

[a] N = number of participants; [b] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317]; [c] p=0.08

Table 32: Effect by whether calcium intake in supplemented group exceeds 1400 mg/day

Site	Calcium intake above 1400 mg/day			Calcium intake below 1400 mg/day		
	No. studies	N[a]	SMD (95% CI)[b]	No. studies	N	SMD (95% CI)
Effect at end of trial						
Femoral neck BMD (g/cm^2)	8	893	+0.07 (-0.06, +0.21)	2	180	+0.04 (-0.25, +0.33)
Lumbar spine BMD (g/cm^2)	8	893	+0.08 (-0.05, +0.21)	3	271	+0.08 (-0.16, +0.32)
Total body BMC (g)	4	407	**+0.21 (+0.01, +0.41)**	5	546	+0.09 (-0.08, +0.26)
Upper limb BMD (g/cm^2)	8	1014	+0.08 (-0.04, +0.21)	4	565	**+0.23 (+0.07, +0.40)**
Effect at end of follow-up after supplement ceased						
Femoral neck BMD (g/cm^2)	3	437	+0.11 (-0.08, +0.30)	2	180	+0.08 (-0.22, + 0.37)
Lumbar spine BMD (g/cm^2)	3	437	+0.05 (-0.13, +0.24)	2	180	-0.09 (-0.39, +0.20)
Upper limb BMD (g/cm^2)	3	437	**+0.25 (+0.06, +0.44)**	3	840	+0.12 (-0.08, +0.31)

[a] N = number of participants; [b] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317]

Table 33: Effect by type of calcium supplementation (milk extract vs. other)

Site	Milk extract			Other supplement		
	No. studies	N[a]	SMD (95% CI)[b]	No. studies	N	SMD (95% CI)
Effect at end of trial						
Femoral neck BMD (g/cm^2)	3	425	+0.09 (-0.10, +0.29)	7	648	+0.05 (-0.10, +0.21)
Lumbar spine BMD (g/cm^2)	3	425	+0.07 (-0.05, +0.21)	8	739	+0.09 (-0.06, +0.23)
Upper limb BMD (g/cm^2)	3	425	+0.03 (-0.17, +0.22)	9	1154	**+0.18 (+0.06, +0.29)**
Effect at end of follow-up after supplement ceased						
Femoral neck BMD (g/cm^2)	2	351	+0.13 (-0.08, +0.34)	3	266	+0.06 (-0.18, +0.30)
Lumbar spine BMD (g/cm^2)	2	351	+0.06 (-0.15, +0.27)	3	266	-0.05 (-0.29, +0.19)
Upper limb BMD (g/cm^2)	2	351	+0.20 (-0.01, +0.41)[c]	4	489	+0.10 (-0.07, +0.28)

[a] N = number of participants

[b] bold denotes statistical significance; SMD = standardised mean difference (95% CI); an SMD of 0.3 is regarded as small[317].

[c] p=0.06

10.4 Discussion

The size of the overall effect of calcium supplementation at the upper limb is small, equating to an approximately 1.8 percentage point greater increase in BMD in the supplemented compared to the control group, an effect which persists after supplementation ceases with a 1.8 percentage point greater increase. While there is a small effect at the upper limb, the resultant increase in BMD is unlikely to result in a clinically significant decrease in fracture risk. It is important to note that this effect did not remain statistically significant when the studies for which imputed outcomes were used were excluded, and it is therefore possible that the upper limb effect may be smaller than indicated in the main analysis. There were no effects seen at other sites at which fracture is common, namely the femoral neck and lumbar spine.

Children with upper limb fractures have been reported to have reduced BMD at the femoral neck, lumbar spine and total body compared to controls with the difference being in the order of 1-5% depending on site of BMD measurement [47]. Other studies examining distal forearm fractures in boys and girls [45, 46] have reported a reduction in ultradistal radius BMD of around 4% in girls and 5% in boys and in 1/3 radius BMD of around 3% in both sexes. Based on the decrease in odds ratio for wrist and forearm fractures observed for each standard deviation increase in lumbar spine BMD [47] the treatment effect observed in this review would result in an approximately 6% decrease in the relative risk of fracture. If this were applied to the peak incidence of all fracture in childhood (about 3% per annum (p.a.) in 15-19 year old boys and 1% p.a. in 10-14 year old girls) [318], the decrease in absolute risk would be at most 0.2% p.a. in boys and 0.1% p.a. in girls. Therefore, while it is possible that the small increase in BMD from calcium supplementation could have an effect on reduction of fracture risk in childhood,

the public health impact of this is likely to be small. Extrapolating these results to assess the potential for reduction in fracture risk in adult life is more problematic. Though the increase in upper limb BMD did persist after cessation of supplementation, the maximum length of follow-up after supplementation was withdrawn was only 7 years [252] and the study participants in even this study had not yet all reached adulthood. The impact of a period of supplementation in childhood on upper limb BMD and fracture risk in later life remains unknown. Even in calcium supplement trials in post-menopausal women, the effect of calcium supplementation on fracture risk is unclear. While BMD increased by around 1.6 to 2 % [319], the point estimate from the meta-analysis of the five studies that included fracture risk as an outcome only suggested a reduction in vertebral fractures (relative risk (RR) 0.79, 95%CI 0.55 to 1.13), and a smaller reduction in risk of non-vertebral fractures (RR 0.86, 95% CI 0.43 to 1.72). However, these results were not significant, probably due to small event numbers. The 2 studies providing data on non-vertebral fracture did not examine upper limb fractures separately as an outcome, probably due to small events numbers. It is not known what relationship exists between radial BMD and fracture risk in the elderly, and in this review, calcium supplementation had no effect on lumbar spine and femoral neck, i.e. the sites known to be predictive of fracture in adults. Therefore, the public health benefits of calcium supplementation in children, either in childhood or in later life appear marginal at best.

The literature pertaining to calcium supplement use in children has been qualitatively reviewed previously [42, 222, 254]. These reviews reported that overall calcium supplementation did appear to have a favourable effect on bone outcomes. One review of intervention studies published up until 1999 [42] reported that calcium supplement use

showed consistent positive effects on bone mass gains in children and adolescents, most consistently at the lumbar spine and total body sites. This review was of only 6 studies, of which 5 were included in our review [248-251, 300]. The sixth study was not included in our review as it was not a randomised controlled trial [289]. A second review [254] included the same six studies with the addition of a seventh [296] and by contrast concluded that increases in BMD occurred mostly at cortical sites, are greater in populations with low baseline calcium intake and do not seem to persist beyond the supplementation period. The most recent review [222] was aimed specifically at determining whether the literature supported the suggestion that dairy products are better for promoting bone integrity that other calcium-containing food sources or supplements. As part of this review the authors described 12 randomised controlled trials with duration of calcium supplementation more than 12 months. They reported that 9 out of 10 trials of calcium supplementation by non-dairy sources showed an increase in bone outcomes and 1 showed no effect and that the three trials of dairy products showed slight effects. None of these latter three trials met the inclusion criteria for our review, as they were not placebo controlled [253, 269] or did not have adequate randomisation [289]. In our review four studies used milk extract supplementation [252, 263, 264, 294]. In contrast to the qualitative reviews, the results of our more robust and more current and complete quantitative systematic review does not support the findings that calcium supplementation has clinically significant beneficial effects in children for bone outcomes or that a particular type of calcium supplementation has more effect on bone than any other.

Subgroup analyses demonstrated little effect modification across the subgroups tested, as one would expect given the lack of heterogeneity overall in the included studies. The consistently greater effects seen in females compared to males across all sites of bone

outcome measurement at the end of supplementation, though not statistically significant, are suggestive of a sex difference in the response of BMD and BMC to calcium supplementation. There were few studies on which to base an assessment of whether this sex difference persisted with withdrawal of supplementation, but on the available data the differences did not persist. The treatment effect on upper limb BMD in the single study performed in an African population was greater than that observed in either Caucasian or Chinese populations, but again not significantly so. Given that this was in a single study, some caution is needed in interpreting this result. The difference in effect may be explained by genetic factors, but the result could also be confounded by dietary, physical activity or other environmental factors.

It is interesting that there were no differences in treatment effects observed between shorter and longer studies. It has been hypothesised that calcium supplementation reduces bone remodeling rather than or as well as increasing bone modelling, thus accounting for the transient benefit of calcium supplementation seen in some individual studies [221]. If bone remodeling was affected by calcium supplementation more than bone modelling, one would expect the difference between treatment effects in shorter versus longer studies to be small, in other words that as the duration of supplementation increased, the rate of increase in BMD/BMC would drop. This is consistent with our data. However, one would also expect that after supplementation ceased there would be a decrease in treatment effect. This is observed in our data for total body BMC but not at the upper limb, which is the only site where an overall treatment effect was observed during supplementation. The reason for this inconsistency between sites is not clear.

During supplementation, the magnitude of changes in bone density outcomes were similar whether the total calcium intake in the intervention arms of the studies did or did not exceed the estimated threshold below which skeletal accumulation varies with intake. This observation supports the concept of a calcium threshold: exceeding the threshold would not be expected to result in greater bone deposition. However, this analysis cannot confirm the magnitude of the threshold; it is possible that it is lower than the threshold proposed in the literature and which was used in this analysis.

The sensitivity analyses performed indicated that the overall review results if anything may have overestimated the treatment effects for the upper limb after calcium supplementation had ceased. Otherwise, the sensitivity analyses had little effect on the review results and do not alter the overall conclusion of the review that the public health benefits of calcium supplementation in children, either in the short-term or long-term, appear marginal at best.

This review has several limitations. No studies in this review measured fractures as an outcome. This is not surprising as a RCT examining fracture outcomes would require a large cohort of children followed for a lengthy period of time to have sufficient power and fracture events to detect an effect on fracture risk. However, this does add to the difficulty of interpreting the clinical and public health significance of the results. The studies selected intentionally did not include trials in children with medical conditions or on medications that might affect bone metabolism. Therefore, the results of this review should not be extrapolated to children with such conditions. Metaregression could not be performed in this review due to the small number of studies. However, in the absence of heterogeneity this is not a significant limitation. While there was no

heterogeneity at any site, subgroup analyses identified areas in which there were gaps in studies in this review, particularly where studies have limited the number of sites measured for their outcomes. There were few studies in which participants could be analysed by whether they were purely post-pubertal and only a single study with only an upper limb outcome in purely peripubertal children. Given that it appears that calcium accumulation in the skeleton accelerates during puberty [320, 321] the absence of sufficient data in the peripubertal period is an important gap to be filled by further research. Other gaps were related to ethnicity and the impact of physical activity. Relatively few studies were in non-Caucasian populations, which resulted in single studies with smaller numbers of participants for some outcomes in ethnicity subgroups. For example, at the femoral neck there was only a single study of Arabs/Jews with a wide confidence interval for the point estimate, though the magnitude of the treatment effect point estimate was larger than that seen in Caucasians. While no effect modification by physical activity was observed, there were only 2 studies to assess this at the lumbar spine, femoral neck and upper limb. Individual results from studies which could not be included in the meta-analysis suggest that effect modification could occur at other sites, but more studies are needed to assess this. It has been suggested that areal BMD only partly corrects for bone size and that adjustment of BMC for bone area, weight and height is desirable [322]. Only 3 studies provided such size adjusted data [292, 293, 296] and so this outcome was not included in the meta-analysis. However, qualitatively the outcomes of these 3 studies were similar, whether they were analysed using BMD or size-adjusted BMC.

In conclusion, while there is a small effect of calcium supplementation at the upper limb, the resultant increase in BMD is unlikely to result in a clinically significant

decrease in fracture risk. The results of this review do not support the use of calcium supplementation in healthy children as a public health intervention. However, these results cannot be extrapolated to children with medical conditions affecting bone metabolism. The absence of sufficient data in the peripubertal period is an important gap to be filled by further research. Long-term calcium supplement studies over the period of peak bone mineral content velocity, perhaps particularly in children with low calcium intake, would be desirable.

Chapter 11: Summary and Future Directions

Osteoporosis is a disease of significant public health importance. Though it manifests most often in the elderly, through fracture, prevention by maximising peak bone mass potentially can begin in childhood. This and prevention by slowing premenopausal bone loss to maintain peak bone mass are both important potential osteoporosis prevention strategies. This thesis explored potential approaches to implementing these strategies in five ways.

Firstly, by examining the baseline data from a randomised controlled trial of individualised bone density feedback coupled with either a leaflet or a group education intervention, we were able to confirm that, as found in other studies, daily calcium intake was low in this random population-based sample of premenopausal women, with 60% of women not meeting the RDI for calcium of 800 mg from dietary sources. We identified subgroups of premenopausal women who are at greater risk of not meeting their RDI for calcium, namely women from a household where the main financial provider was unemployed and women whose highest achieved education level was to grade ten or less. Importantly, other sociodemographic variables are also independently able to explain a significant proportion of the variation in calcium intake. Dietary calcium intake is positively associated with levels of calcium-specific osteoporosis knowledge and calcium-specific osteoporosis self-efficacy (all $p < 0.05$). Women drinking more than 300 ml of milk per day were more likely to meet the RDI for calcium (OR 11.1,95%CI 6.6-18.7). By identifying risk factors for low calcium intake, this information could help target public health strategies aimed at improving the calcium intake of women in this age group. Such health promotion programs also need to specifically address how to approach the sub-group of women who have low

milk intake, with the aim of either increasing consumption of milk or encouraging calcium intake from other sources.

Secondly, we performed a randomised controlled trial to determine the effects of feedback of different levels of fracture risk through individualised bone mineral density (BMD) feedback and leaflet vs. group education on osteoporosis preventive behaviour and 2-year change in BMD in pre-menopausal women. Women who had feedback of low BMD had a greater increase in femoral neck BMD than those with normal BMD (1.6% p.a. vs. 0.7% p.a., p=0.0001), but there was no difference in lumbar spine BMD change between these groups (0.1% p.a. vs. 0.08% p.a., p=0.9). Both educational interventions had similar increases in femoral neck BMD (Leaflet = +1.0% p.a., Osteoporosis self-management course = + 1.3% p.a., p=0.4). Femoral neck BMD change was only significantly associated with starting calcium supplements (1.3 % p.a, 95%CI +0.49, +2.17) and persistent self-reported change in physical activity levels (0.7% p.a., 95%CI +0.22, +1.22). Women receiving feedback of a low T-score result were also more likely to commence calcium supplement use and to report changes in physical activity. This study demonstrates that bone density feedback with minimal patient education in premenopausal women is effective at increasing hip but not lumbar spine bone density and that this effect appears to be mediated by changes in physical activity and calcium supplement usage. While this provides further support for the usefulness of individualised bone density feedback as a health promotion intervention, and the period of follow up in this study is greater than has been reported in previous studies, it is still unclear whether this 2-year change in both behaviours and BMD will persist to provide sustained effects in the long-term. Longer-term follow-up is needed

to confirm any lasting positive effects on BMD from ongoing calcium supplement use and physical activity changes.

A third approach was to assess whether feedback of different levels of fracture risk through individualised bone mineral density (BMD) feedback and leaflet vs. group education had potential to impact on calcium intake and physical activity in the children of the mothers in the study. We assessed maternal report of changing their children's behaviours. Receiving small group education was associated with mothers' report of increasing children's calcium intake (odds ratio 2.3, 95% confidence interval 1.4, 3.8), as was low T-score feedback (odds ratio 2.0, 95% confidence interval 1.2, 3.3). Mothers who increased their own physical activity more often reported increasing both physical activity (odds ratio 2.7, 95% confidence interval 1.5, 5.0) and calcium intake in their children (odds ratio 2.2, 95% confidence interval 1.3, 3.7). Mothers who commenced calcium supplements more often reported increasing children's calcium intake (odds ratio 2.6, 95% confidence interval 1.0, 6.7) but not physical activity.

These results demonstrate that children's calcium intake and physical activity may both be influenced through their mothers and provide the first evidence from a prospective trial that an exclusively parent-focused intervention may be able to improve children's physical activity, though this occurred only in those children whose mothers had changed their own physical activity behaviour. The maternally-reported children's behaviour changes in this study have the potential to increase bone mass and reduce fracture risk in children, as well as increase peak bone mass with its implications for long-term fracture reduction. In addition, if the behaviour changes track into adult life, there are potential benefits for the prevention of osteoporosis through reducing age-

related bone loss, and for the prevention of other chronic diseases whose incidence could be reduced by increased calcium intake and/or increased physical activity, such as cardiovascular disease, obesity and diabetes mellitus. However, while these results support further research to examine parent-focused approaches to lifestyle behavioural change in children, clearly there is a need to confirm these results with objective measures of the behavioural outcomes, and with measures of children's bone mineral density, in future research.

Fourthly, because one of the limitations of the third approach described above was the lack of detailed information about the ways mothers went about changing their children's behaviour, we undertook a qualitative study aimed at describing the strategies and approaches used by mothers to improve calcium intake and physical activity behaviours in their children, in order to inform the development of practical and efficacious health promotion strategies in children. In this study, mothers described a variety of specific dietary changes they made to increase their children's calcium intake. They also described general approaches to improving both calcium intake and physical activity such as: raising awareness of the importance of calcium; ensuring calcium-rich foods were accessible; assessing their children's likes and dislikes and working within these; role modeling; information provision; taking a balanced approach to attempting behaviour change; and encouraging activities that they could do with their children. Mothers described the general importance of a having a balanced diet and lifestyle, rather than specifically for osteoporosis.

This study shows that even without specific guidance, mothers are adept at identifying barriers to change and developing strategies to apply to changing lifestyle behaviours in

their children. The study results provide practical suggestions for dietary changes to include in future interventions, as well as identifying more general strategies and issues to consider when designing interventions to promote lifestyle behavioural change in children. The results also provide further support for considering parent-focused approaches to the difficult issue of improving lifestyle behaviours in children in future research.

Lastly, a systematic review of calcium supplementation for improving bone mineral density in children was performed to assess the effectiveness of this as a potential strategy to increase peak bone mass. The results of this showed that while there is a small effect of calcium supplementation in the upper limb, the increase in BMD which results is unlikely to result in a clinically significant decrease in fracture risk. The results do not support the use of calcium supplementation in healthy children as a public health intervention. However, the results cannot be extrapolated to children with medical conditions affecting bone metabolism, as the studies included in the review were only in healthy children. The review also identified areas in which there were gaps in current research. There were few studies in which participants could be analysed by whether they were purely post-pubertal and only a single study with only an upper limb outcome in purely peripubertal children. Given that it appears that calcium accumulation in the skeleton accelerates during puberty [320, 321] the absence of sufficient data in the peripubertal period is an important gap to be filled by further research. Relatively few studies were in non-Caucasian populations, which resulted in single studies with smaller numbers of participants for some outcomes in ethnic subgroups. For example, at the femoral neck there was only a single study of

Arabs/Jews with a wide confidence interval for the point estimate, though the magnitude of the treatment effect point estimate was larger than that seen in Caucasians.

In conclusion, this thesis has provided considerable information to inform further research into approaches to osteoporosis prevention in premenopausal women and children. Directions for further research suggested by the thesis findings include:

(1) determining whether the observed effects of bone density feedback on women's behaviour and BMD persist in the long-term;

(2) developing and testing a specific mother-focused education process to promote behavioural change in children;

(3) testing (2) combined with bone density feedback to mothers in children, with objective measures of behaviour and BMD performed in children;

(4) investigating the effects of calcium supplementation in children during the period of maximal bone acquisition velocity in the peripubertal stage of development.

(5) examining the roles of nutrients other than calcium in bone development in children, such as fruit and vegetables and vitamin D, given that the impact of calcium supplementation in children is small.

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Appendices

Appendix 1: Calcium Food Frequency Questionnaire

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FOOD FREQUENCY QUESTIONNAIRE FOR CALCIUM INTAKE

Instructions for completing questionnaire:

- Please write in block letters using a black pen (if possible)
- Consider your usual dietary habits over the past 12 months.
- Indicate your response by filling in the circle next to the most appropriate answer or by writing clearly in the boxes or space provided.

Example:

Shade Circles Like This--> ●

Not Like This--> ⊗ ✓

Date : / / DOB: / /

First Name :

Surname :

Maiden Name :

Address:

City: Postcode:

Home Phone: Work Phone:

Mobile:

Friend/relative contact details (not living at home address)

Firstname:

Surname:

Relationship Home Phone:

Mobile Phone Work Phone:

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Please record YOUR intake of the following foods:

MILK

1. How much milk in total do you usually use each day for yourself?

None ..... O
Less than 150 mls .. O
150 to 300 ..... O
300 to 600 mls ..... O
600 mls to 1 litre ..... O
More than one litre .. O

2. If you eat breakfast cereal how much milk do you usually add?

None ..... O
1/4 cup ..... O
1/2 cup ..... O
1 cup ..... O
more than one cup .. O

3. How many cups of tea or coffee with milk do you usually drink each day? ☐☐

4. What type of milk do you usually drink?

No Milk ..... O
Whole milk ..... O
Diet lite ..... O
Light start ..... O
Form ..... O
Skim ..... O
Hi-lite ..... O
Physical ..... O
Soy Milk ..... O
Other ..... O

CHEESE

5. What type of cheese do you usually eat? Please write each type eg cheddar

How much of the following foods do you eat each DAY?

Food Type	Amount per DAY	Equivalents
EXAMPLE *Wholemeal bread*	*7 slices per day*	*1 slice = 25 g*
6. BREAD Wholemeal bread	☐☐ Slices	1 slice = 25 g
White bread or other	☐☐ Slices	1 slice = 25 g
7. YOGHURT Natural yoghurt	☐☐☐☐ grams	1 small carton = 200 g 1 tablespoon = 30 g
Fruit yoghurt	☐☐☐☐ grams	1 small carton = 200 g 1 tablespoon = 30 g

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How much of the following foods do you eat each WEEK?

Food Type	Amount per WEEK	Equivalents
EXAMPLE *Muesli*	*13 tablespoons per week*	*3 tablespoons = 60 g*
7. CHEESE Hard / tasty cheese	☐☐ Slices	1 slice = 30 g
Soft / Cream / Cottage Cheeses	☐☐☐☐ g	1 small carton = 250g
8. ICECREAM	☐☐☐☐ grams	1 scoop = 50 g
9. EGGS	☐☐ large or ☐☐ medium	1 large = 60 g 1 medium = 45 g
10. FISH Tinned salmon	☐☐☐☐ grams	1/2 cup = 120 g
Tinned sardines	☐☐☐☐ grams	4 - 5 sardines = 60 g
Prawns / Shrimps	☐☐☐☐ grams	3 - 4 pieces = 90 g
Scallops	☐☐☐☐ grams	5 - 6 = 90 g
White Fish	☐☐☐☐ grams	1 medium fillet = 100 g
11. CEREAL FOODS Muesli	☐☐☐☐ grams	3 tablespoons = 60 g
All Bran Cereal	☐☐☐☐ grams	2 tablespoons = 10 g
Sweet biscuits / crackers	☐☐☐ biscuits	1 biscuit = 15 g
Chocolate biscuits	☐☐☐ biscuits	1 biscuit = 15 g
Plain Cake	☐☐☐ slices	1 slice = 40 g
12. FRUITS / VEG. / NUTS Spinach / Silver Beet	☐☐☐☐ grams	1/2 cup = 60 g
Dried Fruits	☐☐☐☐ grams	1 tablespoons = 15 g
Peanuts	☐☐☐☐ grams	18 - 20 nuts = 15 g
13. MISCELLANEOUS Chocolate	☐☐☐☐ grams	4 squares = 20 g
Orange Juice	☐☐ glasses or ☐☐☐☐ mls	1 large glass = 200 ml
14. ALCOHOL White wine	☐☐ glasses or ☐☐☐☐ mls	1 glass = 100 ml
Red wine	☐☐ glasses or ☐☐☐☐ mls	1 glass = 100 ml
Beer	☐☐ glasses or ☐☐ stubbies	1 stubby = 375 mls 1 glass = 200 ml

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15. Do you take any calcium or multivitamin tablets? O Yes O No

If so please specify type, amount and frequency.

16. Do you take any antacids or indigestion tablets? O Yes O No

If so please specify type, amount and frequency.

Appendix 2: Physical Activity Questionnaire

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PHYSICAL ACTIVITY QUESTIONNAIRE

Instructions for completing questionnaire:

Please write in block letters using a black pen (if possible)

Indicate your response by filling in the circle next to the most appropriate answer or by writing clearly in the boxes or space provided.

Example:

Shade Circles Like This--> ●

Not Like This--> ⊗ ✓

For purposes of this questionnaire consider your physical activity over the past 12 months.

A. On how many days during the last 14 days did you spent at least 20 minutes doing strenuous exercise?
E.g. bicycling, brisk walking, jogging, aerobics, etc that was severe enough to raise your pulse rate, cause you to breathe faster.

(1) No days ..... O
(2) 1 to 2 days ..... O
(3) 3 to 5 days ..... O
(4) 6 to 8 days ..... O
(5) 9 or more days ..... O

B. On how many days during the last 14 days have you spent at least 20 minutes doing light exercise?
E.g. walking, light housework, slow bicycling, etc. Exercise which was not severe enough to cause a pulse rate rising and or breathing increase.

(1) No days ..... O
(2) 1 to 2 days ..... O
(3) 3 to 5 days ..... O
(4) 6 to 8 days ..... O
(5) 9 or more days ..... O

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C. During a normal week, how many hours a day do you spend watching T.V. or videos?

(1) No hours a day ..... O
(2) 1 hour or less a day ..... O
(3) 2 to 3 hours a day ..... O
(4) 4 to 5 hours a day ..... O
(5) 6 or more hours a day ..... O

D. During the last 12 months, how many team or individual sports activities did you participate in either on a competitive or professional level? E.g. tennis, netball or golf.

(1) No sports or activities ..... O
(2) 1 sport or activity ..... O
(3) 2 sports or activities ..... O
(4) 3 sports or activities ..... O
(5) 4 or more sports or activities O

What sports or activities did you participate in?

1. [ ] 2. [ ]
3. [ ] 4. [ ]
5. [ ] 6. [ ]
7. [ ]

E. Please tick off all the sports or activities which you participated in more than 10 times during the last 12 months. Please include team sports.

Aerobics ..... O
Basketball ..... O
Netball ..... O
Volleyball ..... O
Bicycling ..... O
Bowling ..... O
Dancing ..... O
Gardening ..... O
Bushwalking ..... O
Rollerblading ..... O
Swimming ..... O
(Laps or water sports like water polo or underwater hockey)

Power walking ..... O
Jogging ..... O
Soccer ..... O
Softball ..... O
Hockey ..... O
Tennis ..... O
Squash ..... O
Badminton ..... O
Gym-work weight training . O
Golf ..... O

Any other activities or sports which are not mentioned here [ ]

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Appendix 3: The Osteoporosis Knowledge Assessment Tool

Questionnaire on Osteoporosis

Reg #: ☐☐☐

Please answer each of the following questions with either True, False or Don't know.

Shade Circles Like This--> ●
Not Like This--> ⊗ ✓

1. Osteoporosis leads to increased risk of bone fractures.	O True	O False	O Don't know
2. Osteoporosis usually causes symptoms (e.g. pain) before fractures occur.	O True	O False	O Don't know
3. Having a higher peak bone mass at the end of childhood gives **no** protection against the development of osteoporosis in later life.	O True	O False	O Don't know
4. Osteoporosis is more common in men.	O True	O False	O Don't know
5. Cigarette smoking can contribute to osteoporosis.	O True	O False	O Don't know
6. White women are at highest risk of fracture as compared to other races.	O True	O False	O Don't know
7. A fall is just as important as low bone strength in causing fractures.	O True	O False	O Don't know
8. By age 80, the majority of women have osteoporosis.	O True	O False	O Don't know
9. From age 50, most women can expect at least one fracture before they die.	O True	O False	O Don't know
10. Any type of physical activity is beneficial for osteoporosis.	O True	O False	O Don't know
11. It is easy to tell whether I am at risk of osteoporosis by my clinical risk factors	O True	O False	O Don't know
12. Family history of osteoporosis and fractures strongly predisposes a person to osteoporosis.	O True	O False	O Don't know
13. An adequate calcium intake can be achieved from two glasses of milk a day.	O True	O False	O Don't know
14. Sardines and broccoli are good sources of calcium for people who cannot take dairy products.	O True	O False	O Don't know
15. Calcium supplements alone can prevent bone loss.	O True	O False	O Don't know
16. Alcohol in moderation has little effect on osteoporosis.	O True	O False	O Don't know
17. A high salt intake is a risk factor for osteoporosis.	O True	O False	O Don't know
18. There is a small amount of bone loss in the ten years following the onset of menopause.	O True	O False	O Don't know
19. Hormone therapy prevents further bone loss at any age after menopause.	O True	O False	O Don't know
20. There are no effective treatments for osteoporosis available in Australia resent.	O True	O False	O Don't know

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Appendix 4: The Osteoporosis Self-efficacy Scale and Stage of Change

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Reg #: ☐☐☐

Osteoporosis Self-Efficacy Scale

We are interested in learning how confident you feel about dong the following activities. We all have different experiences, which will make us more or less confident in doing the following things. Thus, there are no right or wrong answers to this questionnaire. It is your opinion that is important. In this questionnaire, EXERCISE means activities such as walking, swimming, golfing, biking and aerobic dancing.

Please fill the circle of the option that best describes your confidence level.

Shade Circles Like This--> ●

Not Like This--> ⊗ ✓

If it were recommended that you do any of the following THIS WEEK, how confident or certain would you be that you could:

1. Begin a new or different exercise program
   O Not at all confident O Mildly Confident O Confident O Very Confident
2. Change your exercise habits
   O Not at all confident O Mildly Confident O Confident O Very Confident
3. Summon up the effort required to exercise
   O Not at all confident O Mildly Confident O Confident O Very Confident
4. Perform exercises even if they are difficult
   O Not at all confident O Mildly Confident O Confident O Very Confident
5. Exercise for the appropriate length of time
   O Not at all confident O Mildly Confident O Confident O Very Confident
6. Do the type of exercises that you are supposed to do
   O Not at all confident O Mildly Confident O Confident O Very Confident
7. Increase your calcium intake
   O Not at all confident O Mildly Confident O Confident O Very Confident
8. Change your diet to include more calcium rich foods
   O Not at all confident O Mildly Confident O Confident O Very Confident
9. Eat calcium rich foods as often as you are supposed to
   O Not at all confident O Mildly Confident O Confident O Very Confident
10. Select appropriate foods to increase your calcium intake
    O Not at all confident O Mildly Confident O Confident O Very Confident
11. Stick to a diet which gives an adequate amount of calcium
    O Not at all confident O Mildly Confident O Confident O Very Confident
12. Obtain foods that give an adequate amount of calcium
    O Not at all confident O Mildly Confident O Confident O Very Confident

Stage of Change Questions

. How would you describe your dietary calcium intake?

- O I do not think that my present dietary calcium intake is adequate and do not intend to increase it.
- O I am thinking about increasing my present dietary calcium intake
- O I have decided to start increasing my present dietary calcium intake in the next month
- O I have been increasing my dietary calcium intake for less than six months now
- O I have been increasing my dietary calcium intake for more than six months now
- O I have an adequate or high dietary calcium intake and will continue at that high or adequate level

. How would you describe your physical activity?

- O I am not doing any regular physical activity and do not intend to start.
- O I am thinking about starting some form of regular physical activity.
- O I have decided to start doing regular physical activity in the next month
- O I have been doing regular physical activity for less than six months now.
- O I have been doing regular physical activity for more than six months now.
- O I have maintained an adequate level of physical activity since adolesence

Appendix 5: Children's Behaviour Change

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Osteoporosis LIFESTYLE QUESTIONNAIRE

Instructions for completing questionnaire:

- Please write in block letters using a black pen (if possible)
- Consider your usual dietary habits over the past 12 months.
- Indicate your response by filling in the circle next to the most appropriate answer or by writing clearly in the boxes or space provided.

Example:

Shade Circles Like This--> ●

Not Like This--> ⊗ ✓

Date : ☐☐ / ☐☐ / ☐☐☐☐

Please answer all questions to the best of your ability:

1. Since taking part in the study have you changed any of the following behaviours

(a) **Physical Activity?** O Yes O No

(b) **Smoking?** O Yes O No

If Yes, how many do you now smoke per day? **Number of Cigarettes** ☐☐☐

(c) **Calcium Intake?** O Yes O No

(d) **Calcium Supplement usage?** O Yes O No

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2. If applicable, how important were the following in motivating you to change your behaviour?

(1 = not at all important, 2 = slightly important, 3 = unsure, 4 = important, 5 = very important)

	1	2	3	4	5
(a) Bone Density Result	O	O	O	O	O
(b) Educational information provided?	O	O	O	O	O
(c) Combination of the above?	O	O	O	O	O
(d) Information from a Health Professional outside of the study?	O	O	O	O	O
(e) Other if so please state?	O	O	O	O	O

3. In the last year has your Spouse/Partner changed any of the following?

(a) Calcium intake?	**Increased** O 1	**Decreased** O 2	**Remained the same** O 3
b) Physical Activity?	**Increased** O 1	**Decreased** O 2	**Remained the same** O 3

4. If you have children, in the last year have you changed their :

(a) Calcium intake?	**Increased** O 1	**Decreased** O 2	**Remained the same** O 3
(b) Physical Activity?	**Increased** O 1	**Decreased** O 2	**Remained the same** O 3

7. Comments and feedback on any issues about the study?

ie. Has your participation in the study had any influence on other friends or family members.

Appendix 6: General Measures

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BONE DENSITY STUDY FOR PRE-MENOPAUSAL WOMEN LIVING IN THE HOBART AREA

Instructions for completing questionnaire:

Please write in block letters using a black pen (if possible)

Indicate your response by filling in the circle next to the most appropriate answer or by writing clearly in the boxes or space provided.

Example:

Shade Circles Like This--> ●

Not Like This--> ⊗ ✓

Name: _____

Date of Birth: _____

Todays Date ☐☐ / ☐☐ / ☐☐☐☐

Weight ☐☐☐.☐ kg

Height ☐☐☐ cm

1. Sunlight Exposure

What is the average length of time per day that you spend outside (please fill one circle in each section for summer and winter)

	Summer (Dec/Jan/Feb)		Winter (Jun/Jul/Aug)	
a) Weekdays	Less than two hours per day	O	Less than two hours per day	O
	2 - 3 hours per day	O	2 - 3 hours per day	O
	3 - 4 hours per day	O	3 - 4 hours per day	O
	More than four hours per day	O	More than four hours per day	O
	Summer (Dec/Jan/Feb)		**Winter (Jun/Jul/Aug)**	
b) Weekends	Less than two hours per day	O	Less than two hours per day	O
	2 - 3 hours per day	O	2 - 3 hours per day	O
	3 - 4 hours per day	O	3 - 4 hours per day	O
	More than four hours per day	O	More than four hours per day	O

2. Is the main financial provider in your household unemployed or on a pension? Yes O No O

3. Are you in paid employment?

No O
Yes (< 20 hours per week) O
Yes (>20 hours per week) O

4. What is your present marital relationship?

Single O
Married, living together O
Married, separated O
Unmarried, living together (defacto) O
Unmarried, not living together O
Divorced O

5. Bone Density Results

	BMD	T Score	BMC
Lumbar Spine			
Femoral Neck			
Total Body			

Lean Mass Fat Mass

6. Leg Muscle Strength Strength #1 ☐☐☐ Strength #2 ☐☐☐

7. Physical work capacity (Endurance Fitness)

If there is no significant increase in the participants heart rate between the second and third minutes of the test then increase the work load to 1.0 Kg and commence readings from there. This is the only time at which a work load of 2.0 Kg will be used.

Minute	Time	Heart Rate	Work Load	Minute	Time	Heart Rate	Work Load
1	☐:☐☐	☐☐☐	0.5	9 / 5	☐:☐☐	☐☐☐	1.5
2	☐:☐☐	☐☐☐	0.5	10 / 6	☐:☐☐	☐☐☐	1.5
3	☐:☐☐	☐☐☐	0.5	11 / 7	☐:☐☐	☐☐☐	1.5
4	☐:☐☐	☐☐☐	0.5	12 / 8	☐:☐☐	☐☐☐	1.5
5 / 1	☐:☐☐	☐☐☐	1.0	9	☐:☐☐	☐☐☐	2.0
6 / 2	☐:☐☐	☐☐☐	1.0	10	☐:☐☐	☐☐☐	2.0
7 / 3	☐:☐☐	☐☐☐	1.0	11	☐:☐☐	☐☐☐	2.0
8 / 4	☐:☐☐	☐☐☐	1.0	12	☐:☐☐	☐☐☐	2.0

Incomplete Bike Test

Equipment malfunction O
Technique difficulties O
Refused to continue O
Elevated pulse rate O
Physical restrictions O
Abnormal Heart Rate O

General Comments

Difficulty in maintaining RPM O
Erratic RPM O
Physical Limitations O

Comments

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Appendix 7: References excluded from the systematic review.

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Appendix 8: Reasons for exclusion of references

Study	Reason for exclusion
Abrams 2001	Not a randomised controlled trial
Adiyaman 2004	Not a randomised controlled trial
Albertson 1997	Not a randomised controlled trial
Ali 2001	Not a randomised controlled trial
Anderson 2001	Not a randomised controlled trial
Andon 1994	Not a randomised controlled trial
Anonymous 1992	Not a randomised controlled trial
Anonymous 1993a	Not a randomised controlled trial
Anonymous 1993b	Not a randomised controlled trial
Anonymous 1994	Not a randomised controlled trial
Anonymous 1997a	Not a randomised controlled trial
Anonymous 1997b	Not a randomised controlled trial
Anonymous 1998	Not a randomised controlled trial
Anonymous 2000	Not a randomised controlled trial
Anonymous 2004	Not a randomised controlled trial
Antoniazzi 2003	Condition affecting bone metabolism (participants treated with gonadotrophin-releasing hormone agonist)
Antoniazzi 1999	Condition affecting bone metabolism (participants treated with gonadotrophin-releasing hormone agonist)
Appleby 1998	Not a randomised controlled trial
Ausenhus 1988	Not a randomised controlled trial

Badenhop 2004	Not a randomised controlled trial
Barker 1998	No placebo used
Barr 1998	Not a randomised controlled trial
Barr 2001	Not a randomised controlled trial
Bateson 2002	Not a randomised controlled trial
Berthier 1994	Not a randomised controlled trial
Black 2002	Not a randomised controlled trial
Blalock 2002	No calcium intervention
Bonjour 1999	Not a randomised controlled trial
Bonofiglio 2004	Not a randomised controlled trial
Boot 1997	Not a randomised controlled trial
Bourges	Not a randomised controlled trial
Brown 2004	No calcium intervention
Burckhardt 2001	Not a randomised controlled trial
Cadogan 1997	No placebo used
Carter 2001	Not a randomised controlled trial
Chan 1987	Trial in lactating adolescents ie condition affecting bone metabolism
Chan 1991	Not a randomised controlled trial
Chan 1995	No placebo used
Cheng 1999	Not a randomised controlled trial
Chevalley 2004	Not a randomised controlled trial
Clements 1991	Not a randomised controlled trial

DeBar 2004	No calcium intervention
DiMeglio 2005	No calcium intervention
Dowd 2001	Not a randomised controlled trial
Du 2002	Not a randomised controlled trial
Du 2004	No placebo used
Edwards 1998	Not a randomised controlled trial
El-Husseini 2004	Condition affecting bone metabolism (renal transplantion)
Elgan 2002	Not a randomised controlled trial
Feskanich 1997	Not a randomised controlled trial
Fischer 1999a	No placebo
Fischer 1999b	Duplicate paper to Fischer 1999a
Fisher 2004	Not a randomised controlled trial
Fujita 1992	Not a randomised controlled trial
Gharib 2004	Not a randomised controlled trial
Gibbons 2004	Active placebo used (400 mg calcium)
Ginty 2004	Not a randomised controlled trial
Goulding 2004	Not a randomised controlled trial
Griffiths 1998	Not a randomised controlled trial
Grossklaus 1998	Not a randomised controlled trial
Gulati 2005	Not a randomised controlled trial
Hampton 2004	Not a randomised controlled trial
Harel 1998	Not a randomised controlled trial
Henderson 1994	Not a randomised controlled trial

Hidvegi 2003	Not a randomised controlled trial
Homik 2005	Not a randomised controlled trial
Hoppe 2000	Not a randomised controlled trial
Hosokawa 1996	Not a randomised controlled trial
Howat 2001	Not a randomised controlled trial
Iki 2003	Not a randomised controlled trial
Ilich 1996	Not a randomised controlled trial
Infante 2000	Not a randomised controlled trial
Kalkwarf 1997	Adult participants and participants lactating
Kalkwarf 2003	Not a randomised controlled trial
Kalusk 2001	Not a randomised controlled trial
Kanis 1994	Not a randomised controlled trial
Kardinaal 1999	Not a randomised controlled trial
Kasper 2001	Not a randomised controlled trial
Kerstetter 1995	Not a randomised controlled trial
Koenig 2000	Not a randomised controlled trial
Kowalski 2004	Not a randomised controlled trial
Kreipe 1995	Not a randomised controlled trial
Kubota 2003	Not a randomised controlled trial
Kun 2001	Not a randomised controlled trial
Lappe 2004	No bone outcome measures (trial of calcium effect on wieght gain)
LaRosa 2004	Not a randomised controlled trial

Lau 1992	No placebo and no randomisation
Lau 2004	No placebo used
Lee 1993	Not a randomised controlled trial
Lee 2003	Not a randomised controlled trial
Levers-Landis 2003	Not a randomised controlled trial
Li 2002	No placebo used
Lloyd 2000	Not a randomised controlled trial
Lloyd 2002	Not a randomised controlled trial
Lysen 1997	Not a randomised controlled trial
Ma 2004	Not a randomised controlled trial
Mackelvie 2001	Not a randomised controlled trial
Magee 1996	No placebo used
Maggiolini 1999	Not a randomised controlled trial
Mahana 1988	Not a randomised controlled trial
Mallet 2000	Not a randomised controlled trial
Mallet 2003	Not a randomised controlled trial
Marrero 2004	Not a randomised controlled trial
Martin 2004	Not a randomised controlled trial
Matkovic 1990	Inadequate randomisation
Matkovic 2002	Not a randomised controlled trial
McCulloch 1990	Not a randomised controlled trial
Meier 2004	Participants were adults.
Merrilees 2000	No placebo used

Meschino 2004	Not a randomised controlled trial
Moelgaard 2001	Not a randomised controlled trial
Monge 2001	Not a randomised controlled trial
Moya 1997	Not a randomised controlled trial
Moyer-Mileur 2003	Intervention combined vitamin D and calcium with no capacity to seperate calcium effect.
Naunton 2004	Not a randomised controlled trial
Neville 2002	Not a randomised controlled trial
New 1998	Not a randomised controlled trial
NIH 2001	Not a randomised controlled trial
Novotny 2004	Not a randomised controlled trial
Nowson 1995	Duplicate data (conference abstract)
O' Brien 1998	Not a randomised controlled trial
Oellingrath 1989	Not a randomised controlled trial
Ohgitani 1997	No BMD or BMC outcomes
Oria 2003	Not a randomised controlled trial
Parr 2002	Not a randomised controlled trial
Pena 2004	Not a randomised controlled trial
Peterson 2000	No calcium intervention
Piaseu 2002	No calcium intervention
Picard 1988	Not a randomised controlled trial
Portsmouth 1994	Not a randomised controlled trial
Prestridge 1993	Condition affecting bone metabolism (very low birth weight

	infants)
Prynne 2004	Not a randomised controlled trial
Purdie 1994	Not a randomised controlled trial
Recker 1993	Not a randomised controlled trial
Reid 1998	Not a randomised controlled trial
Remer 2002	Not a randomised controlled trial
Renner 1991a	Not a randomised controlled trial
Renner 1991b	Not a randomised controlled trial
Renner 1994	Not a randomised controlled trial
Renner 1998	No placebo or randomisation
Roberts 2000	Not a randomised controlled trial
Robertson 2005	Not a randomised controlled study
Roux 1995	Not a randomised controlled trial
Rozen 2001	Not a randomised controlled trial
Ruiz 1995	Not a randomised controlled trial
Runyan 2003	Not a randomised controlled trial
Sagara 2002	Not a randomised controlled trial
Saggese	Not a randomised controlled trial
Sakkers 2004	No calcium intervention
Scholz 1993	Not a randomised controlled trial
Schonau 2004	Not a randomised controlled trial
Smart 1994	Not a randomised controlled trial
Solomons 1996	No a randomised controlled study

Soroko 1994	Not a randomised controlled trial
Specker 1997	No placebo
Specker 1999	No calcium intervention
Specker 2002	Duplicate data (conference abstract)
Stallings 1994	Not a randomised controlled trial
Szumera 2004	Not a randomised controlled trial
Taha 2001	Not a randomised controlled trial
Teegarden 1994	Not a randomised controlled trial
Teegarden 1999	Not a randomised controlled trial
Teesalu 1996	Not a randomised controlled trial
ter Meulen 2004	Condition affecting bone metabolism (renal transplantation)
Torres 2004	Condition affecting bone metabolism (renal transplanation)
Tortolani 2002	Not a randomised controlled trial
Tounian 2003	Not a randomised controlled trial
Tsukahara 1997	Not a randomised controlled trial
Tucker 2003	Not a randomised controlled trial
Turner 1992	Not a randomised controlled trial
Turner 2000	Not a randomised controlled trial
Tussing 2005	Not a randomised controlled trial
Tylavsky 1992	Not a randomised controlled trial
Ulrich 1996	Not a randomised controlled trial
Valerio 2004	Not a randomised controlled trial
VandenBergh 1995	Not a randomised controlled trial

Vigano 2004	Not a randomised controlled trial
Volek 2003	Outcomes measured at less than 6 months from baseline
Wallace 2002	Not a randomised controlled trial
Wang 1999	Not a randomised controlled trial
Wang 2003	Not a randomised controlled trial
Wastney 2003	Not a randomised controlled trial
Weaver 1999	Not a randomised controlled trial
Welten 1995	Not a randomised controlled trial
Welten 1997	Not a randomised controlled trial
Whiting 2001	Not a randomised controlled trial
Whiting 2004	Not a randomised controlled trial
Winters-Stone 2004	Participants aged > 18 years
Yeste 2004	Not a randomised controlled trial
Zacharin 2004	Not a randomised controlled trial
Zanchetta 1995	Not a randomised controlled trial
Zhang 2003	No placebo used
Zhu 2003	No placebo used
Zhu 2004	No placebo used
Zhu 2004 b	Not a randomised controlled trial
Ziccardi 2004	Not a randomised controlled trial
Zwart 2004	No calcium intervention
Zwiauer 2003	Not a randomised controlled trial